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In the 21st century many branches in medicine can not exist without physicists. Most recent methods in medicine, especially new technologies in cancer diagnostic and treatments, have resulted in a great need for medical physicists in growing number of institutions and hospitals.

There are a certain number of highly qualified and dedicated professionals in medical physics in Macedonia whose work is mainly performed in governmental institutions committed towards medical physics issues. The Association for Medical Physics and Biomedical Engineering (AMPBE) was established in 2000 as the first professional association in Macedonia competent to cope with problems in the fields of medicine, applying methods of physics and biomedical engineering to medical procedures in order to develop tools essential to the physicians that will improve medical care in general.

Three years ago the First National Conference on Medical Physics and Biomedical Engineering was organized by the Association. The idea was to gather all the professionals working in medical physics and biomedical engineering on one place in order to present their work and increase the collaboration among them. Other involved professions such as medical doctors, radiation technologists, engineers and physics professors from the University also took part and contributed to the success of the conference. As a result the Proceedings were published in Macedonian, with summaries in English.
In order to further promote the medical physics amongst scientific community in Macedonia, our society decided to organize THE SECOND CONFERENCE FOR MEDICAL PHYSICS AND BIOMEDICAL ENGINEERING in November 2010, this time with international character. This is an event very suitable for our Association’s 10th anniversary. Thanks to the cooperation of the European Federation of Organisations for Medical Physics (EFOMP), renowned experts took part as Conference’s plenary speakers. This proceeding contains works in different fields presented on the conference orally or as poster presentations.

I want to express my special thanks to the invited lecturers for their immense contribution to the success of the conference.

This scientific event would not be possible without financial support of the selected companies presented here.

I would like to conclude by offering my sincere appreciation to the Scientific Committee and the Organizing Committee for their professional work.

Sonja Petkovska
President of the Association for Medical Physics and Biomedical Engineering
Abstract — An overview of quantitative magnetization transfer (qMT) is given, with focus on cross-relaxation imaging (CRI) as a fast method for quantifying the proportion of protons bound to complex macromolecules in tissue. The procedure for generating CRI maps is outlined, showing examples in the human brain and knee, and discussing the caveats and challenges in generating precise and accurate CRI maps. Finally, several applications of CRI for imaging tissue microstructure are presented.

Keywords – MRI, cross-relaxation imaging, quantitative magnetization transfer, tissue modeling

1. WHAT IS MAGNETIZATION TRANSFER?

In conventional magnetic resonance imaging (MRI), most of the signal comes from hydrogen in water molecules. This hydrogen is highly mobile, with a relatively long $T_2$ relaxation constant (~100 ms). We refer to it as the free pool. In addition to hydrogen in the free pool, there is also hydrogen bound to complex macromolecules, such as proteins, lipids, and sugars. This hydrogen is less mobile, and has a short $T_2$ (on the order of microseconds.) We refer to this as the bound, or the macromolecular pool. Figure 1 shows a diagram of hydrogen in the free and the bound pools.

![Fig. 1: (Left) Hydrogen in water, $T_2 \sim 10-100$ ms. (Right) Hydrogen bound to sphingomyelin, a macromolecule found in myelin $T_2 \sim 10 \mu$s.](image)

It is difficult to image the bound pool directly, due to its short $T_2$. However, an indirect method called magnetization transfer (MT) sensitizes the MR sequence to hydrogen bound to macromolecules [1]. Magnetization transfer imaging was first proposed by Wolff and Balaban in 1989 [2]. The main idea behind it is that the free pool has a very narrow spectrum (on the order of Hz), and the bound pool spectrum is wide (on the order of kHz). Therefore, it is possible to excite the bound pool without perturbing the free pool by applying an MT radio-frequency (RF) pulse. Once the bound pool is excited, the protons bound to macromolecules exchange magnetization with the protons found in free water and reduce the net MR signal. This experiment can be performed with on-resonance [2–5] or off-resonance [6, 7] MT pulses, which can be continuous [2, 3, 6] or pulsed [4, 5, 7].

![Fig. 2: A model for the exchange between the bound (MB) and the free pool (MF). A magnetization transfer RF pulse is applied, which saturates the bound pool (RRFB) but has a very small effect on the free pool (RRFF). When the MT pulse is turned off, both pools recover with their respective $T_1$ relaxation rates ($T_1^B$, $T_1^F$), but there is also magnetization exchange (k) which effectively reduces the net MF magnetization.](image)

Regardless of the pulse used, the excited bound pool interacts with the free pool, effectively reducing its net magnetization. This process of exchange of magnetization between the bound and the free pool is called magnetization transfer, and is schematically described in Fig. 2. Because only the free pool can be imaged directly, the result is a unique type of contrast, which makes regions with high bound pool content appear darker than those with low bound pool content.
1.1. Lineshape and Z-spectrum

The magnetization transfer contrast depends on the frequency at which the MT pulse is applied, and on the lineshape of the imaged tissue. The lineshape is the Fourier Transform of the free induction decay, and it represents the extent to which different RF frequencies affect the magnetization. Its width is inversely proportional to the $T_2$ relaxation time. Therefore, the free pool tends to have a narrow lineshape, and the bound pool has a wide lineshape. The lineshape of the free pool can be modeled by a Lorentzian, whereas the lineshape of the bound pool can be modeled by a Gaussian in phantoms, and a Superlorentzian in tissue [8–10].

On-resonance MT pulses saturate both the bound and the free pool. Off-resonance pulses saturate the bound pool, but only have a small effect on the free pool. After the MT pulse is applied, the free pool magnetization evolves according to a quantitative MT model [11-13]. After a series of MT pulses is applied, a steady state is reached and the net magnetization of the free pool is a fraction of the initial free pool magnetization. This fraction depends on the frequency of the MT pulse and the respective lineshapes of the two pools. Plotting the net magnetization as a function of the frequency of the MT pulse gives the z-spectrum (Fig. 3) of the object of interest.

1.2. Magnetization Transfer Ratio

According to Fig. 3, when an MT pulse is applied around 0 Hz, both the bound pool and the free pool are completely saturated. As the frequency of the MT pulse goes up, the bound pool is still fully saturated (due to its wide lineshape), but the free pool only feels a small direct effect $M_{DIR}$. After the MT pulse, there is magnetization transfer between the free and the bound pool, which results in the free pool losing more of its magnetization ($M_{MT}$). The difference in free pool magnetization before and after an MT pulse is defined as the Magnetization Transfer Ratio (MTR) [7]. So one can think of the MTR as samples of the z-spectrum at different frequencies.

If we define $M_0$ as the initial free pool magnetization, $M_{DIR}$ as the loss of magnetization due to the direct effect of the MT pulse, and $M_{MT}$ as the loss of magnetization due to MT, then:

$$MTR = \frac{M_0 - M_{DIR} - M_{MT}}{M_0} = 1 - \frac{M_{DIR} + M_{MT}}{M_0}$$  \hspace{1cm} (1)

The MTR metric includes contributions from several MR parameters [14, 15], such as the longitudinal relaxation rate ($T_1$), the exchange rate ($k$), and the bound pool fraction (BPF), defined as the fraction of exchanging protons that are bound to macromolecules. Sometimes these parameters combine to mask the magnetization transfer effect. This is the case when an area with decreased BPF has an increase in $T_1$ [16, 17].

1.3. Quantitative Magnetization Transfer (qMT)

In order to decouple the individual contributions of $T_1$, $k$ and BPF from the MTR, a more exact mathematical description of the MT process is needed. The evolution of the free and the bound pool magnetization can be represented by a linear system with several tissue dependent and pulse sequence dependent parameters:

$$\frac{dM_z}{dt} = (A + B)M_z + C$$  \hspace{1cm} (2)

where $A$ is a matrix accounting for the magnetization transfer between the two pools, $B$ represents the direct effect of the MT pulse, and $C$ represents the longitudinal recovery in the absence of external pulses. Equation 3 is an expansion of Eq. 2 that gives a more detailed look at the qMT modeling:
$M_z^F$ and $M_z^B$ are the longitudinal magnetization of the free and the bound pool, which evolve as a function of time. $T_1^F$, $T_2^F$, $T_1^B$, and $T_2^B$ are the relaxation parameters of the free and the bound pool, respectively. BPF is the bound pool fraction, defined as the proportion of exchanging protons bound to macromolecules, and $\kappa$ is the rate of exchange (in $s^{-1}$) between the free and the bound pool. $g(\Delta, T_2^B)$ is the Superlorentizan lineshape of the bound pool. The parameters that depend on the pulse sequence are the off-resonance frequency of the MT pulse ($\Delta$), and the magnitude of the MT pulse ($\alpha_{\text{rms}}$).

Based on this model, several quantitative magnetization transfer (qMT) methods have been proposed [14, 18–22]. While the methodology and terminology used in the above methods differ significantly, their goal is similar - to determine the proportion of protons that are bound to macromolecules, and to quantify the rate of exchange of magnetization between the bound and free protons. There has not been a comprehensive study comparing all of the above methods. Studies comparing the pulsed off-resonance techniques [14, 18–20] suggest that they provide consistent measurements of the macromolecular pool size [23] that are comparable to ex vivo results [24].

This paper focuses on the qMT method proposed by Yarnykh and Yuan in 2004 [25]. Their method uses the term cross-relaxation imaging (CRI) and is a modification of the earlier work by Yarnykh [19]. The main difference is that the new method accounts for the direct effect of the MT pulse on the free pool. We focus on this method because, of all the methods mentioned above, it is the only one that can provide large 3D coverage in a reasonable amount of time, using only product MR sequences readily available on any MR scanner.

![CRI flowchart in the human knee](image)

Fig. 4: CRI flowchart in the human knee

The speed and ease of implementation is achieved at the expense of several model simplifications and approximations. We tested the model in a variety of settings, to make sure that the approximations and the modeling are well-suited to the experiment at hand. What follows is a case study of cross-relaxation imaging which discusses several issues related to the CRI methods and modeling, followed by an overview of potential CRI applications in studying tissue microstructure.

2. CRI: A CASE STUDY

The CRI procedure consists of two sets of scans. First, $T_1$ mapping is performed using a set of four variable flip angle SPGR scans (TR = 20 ms, TE = 2.4 ms, $\alpha$ = 4°, 10°, 20°, 30°) [26].

The $T_1$ mapping is followed by four variable offset frequency MT scans (TR = 32 ms, TE = 2.4 ms, $\alpha$ = 10°, $\Delta$ = 3, 9, 15, 21 kHz). Fermi off-resonance RF pulses are used (8 ms duration, 670° flip angle), and the offset frequencies are chosen so they sample the $z$-spectrum of the scanned object. For example, brain tissue has a narrower $z$-spectrum than cartilage, and this is due to the longer $T_2^B$, the bound pool transverse relaxation rate.

The $T_1$ map is used to generate a synthetic image, called $S_0$, which serves as a reference for the MT scans. Namely, all four MT scans have a signal reduction compared to a reference image when no MT pulse is applied. However, this reference image need not be acquired, as it can be synthesized from the $T_1$ map, using the same TR, TE and flip angle as the MT scans. The $S_0$ image is synthesized from:

$$S = \rho \frac{1 - e^{-\alpha_\text{rms}/T_1}}{1 - e^{-\alpha_\text{rms}/T_2}} \sin \theta$$

where $\rho$ and $T_1$ are obtained from the variable flip angle $T_1$ mapping technique [26], and $\theta$ and TR are the same as for the MT scans.

Avoiding this additional scan results in a significant reduction of scan time, and most of the time this simplification is legitimate. However, in specific situations it is essential that this $S_0$ image be acquired, and not synthesized. Later in the paper we discuss this issue. The prediction model makes $a$ priori assumptions about all unknown parameters except for $k$ and BPF. A non-linear least-squares Levenberg-Marquardt algorithm is used to find the $k$ and BPF values that minimize the prediction error. Figure 4 is a flowchart showing the scans required to generate CRI maps of the human knee.

2.1. CRI Maps in the Human Knee

Figure 5 shows four maps of a single knee slice in vivo. While the cartilage is clearly visible on the $T_1$ and MTR maps, the BPF and $k$ maps provide additional information and enable better differentiation of cartilage. In particular, cartilage and muscle have similar $T_1$ and MTR values, but the BPF values in cartilage are significantly higher than those in muscle (0.25 vs. 0.13). A possible reason for this
difference is that the MTR depends not only on the BPF, but also on several other parameters such as $T_1$ and the exchange rate $k$. Unlike the $T_1$ and the MTR maps, the BPF and $k$ maps also show good contrast in the meniscus.

The CRI maps require accurate sampling of the tissue z-spectrum, so it is beneficial to acquire as many different MT offset frequencies as possible. However, performing this in vivo is difficult because of time constraints and motion artifacts that can occur when scan duration is increased. In order to test the validity of the CRI model, we scanned ex vivo specimens of the human tibia and patella, which have thick cartilage in the knee joint area.

![Figure 5: (Top) A $T_1$ and MTR map. (Bottom) BPF and $k$ map. All four maps clearly outline the cartilage, but the BPF and $k$ map complement the information present in the $T_1$ and MTR map. The red arrow points out the meniscus. In the BPF and $k$ map there is clear differentiation between the white (bright) and red (darker) zone of the meniscus. The green arrow points out a region in cartilage where the MTR is significantly higher. This feature is visible only in the $k$ map, and is not outlined in the BPF or $T_1$ map.](image)

![Figure 6: Reprinted from [30]. A single slice from a tibia specimen, imaged using the CRI protocol. The in-plane resolution is 0.8 x 0.8mm, and the slice thickness is 3mm. Shown are a $T_1$ map (top left), MTR map (top right), $k$ map (bottom left) and BPF map (bottom right).](image)

The MTR, BPF, $k$ and $T_1$ map for a single slice of a tibia ex vivo specimen are shown in Fig. 6. Perpendicular to the cartilage surface, the $T_1$ and the $k$ map vary smoothly in opposite directions. The MTR is relatively flat in comparison, and the BPF map shows a heterogeneous structure that cannot be seen in any of the other CRI maps. The opposing trend between $T_1$ and the cross-relaxation maps ($k$ and BPF) results in a small dynamic range for MTR, which could be the reason for the flatness of the MTR maps, compared to the maps of the individual CRI parameters.

### 2.2. CRI Quality of Fit

To test the CRI fit quality, we acquired 27 scans with different MT offsets, along with the reference $S_0$ image. The total scan time was 75 minutes. As Fig. 7 shows, the MT points sample the entire z-spectrum up to 40.5kHz. At high offset frequencies the bound pool is no longer saturated, and there is no MT effect anymore, so we can assume that the mean MR signal is the same as that of the $S_0$ image acquired without MT. Figure 7 shows that our fit models closely the z-spectrum of cartilage.

![Figure 7: Quality of fit to z-spectrum at a single ROI from the tibia. 27 off-resonance MT scans were acquired, and the absolute numbers from the MR images are represented by colored circles. The line passing through the circles is the fit provided by the two-pool model. For this particular voxel, BPF = 0.18, $k$ = 1.33 s$^{-1}$.](image)

### 2.2.1. CRI Sensitivity to $S_0$ and Scanner Drift

Despite acquiring 27 off-resonance points, inaccuracies in the $S_0$ image can corrupt the BPF map. Figure 8 shows how a voxel can have an artificially high BPF value due to an incorrect value for $S_0$. The points at high offset frequencies should be approaching one, but in the right column, even at high offsets the ratio $S_i/S_0$ is significantly lower. When this is the case, the z-spectrum MT model cannot pass through all the points, because the model assumes that at high frequencies the ratio is 1. As a result, the BPF and $k$ values end up artificially high. One way to mitigate this is to acquire the $S_0$ image, instead of synthesizing it. If possible, the $S_0$ should be acquired right after the last MT scan to ensure that $S_i/S_0$ is close to one. This results in a longer scan time, but ensures a more robust fit.
Fig. 8: The quality of fit for a voxel where $S_0$ is incorrect. The red circles indicate the points used for the fitting procedure. The top image uses 4 points, whereas the bottom fit uses all 27 points. The high offset MT scans do not match $S_0$, so the fit is very sensitive to the subset of points used.

Drifts of the absolute signal value can explain the high CRI variability over time. To check this, we acquired the same set of MT scans several times in a row, and found that the mean signal from the first set of scans was consistently higher than the second set of scans. This can be seen in Fig. 9, where four sets of MT scans were acquired on the same sample twice in a row, without changing any MT parameters and without any breaks between the scans.

One reason for this behavior is that the MT scans are RF intensive, with an RF duty cycle of about 30%. As the RF amplifiers are designed for a 10% duty cycle, during the MT scans they are operating outside of their specifications. The longer the amplifiers are operating in this regime, the harder it is to supply the necessary current. As a result, the current output drops, the $B_1$ amplitude is lower than what the sequence prescribes, and the mean signal decreases.

While this effect is present whenever an MT pulse sequence is played out, one way to mitigate it is to provide breaks between RF intensive scans. For the purposes of our experiment, we recommend interleaving the MT and the $T_1$ mapping scans. As the SPGR scans used for $T_1$ mapping are not RF intensive, they will provide the necessary rest for the RF amplifier.

Figure 9: The repetition of two sets of MT scans in the same sample at four offset frequencies. The first four scans correspond to points on the top, the points on the bottom are from the second set. If the same $S_0$ image is used, the second set of scans will produce higher CRI values, because the additional signal decrease will be interpreted as the MT effect of a larger bound pool.

2.2.2. CRI Sensitivity to $T_1$

$T_1$ mapping is an essential part of the CRI procedure, so the CRI values are very sensitive to the $T_1$ parameter. At 1.5T, the $T_1$ parameter can vary by as much as 10% depending on the precision of the RF transmit ($B_1$) field. Due to the non-linearity of the CRI model, the $T_1$ uncertainty can result in BPF variations of 20%. Figure 10 points out this variability.

While the two BPF maps look very similar visually, the absolute BPF values are about 20% apart, as can be seen from the grayscale colorbars next to the maps. In the absence of precise $T_1$ values, it is difficult to compare BPF values across subjects. However, the relative differences within a BPF map are preserved, so comparisons of values within a subject are valid.

2.2.3. CRI Sensitivity to the a priori Parameters

The previous sections discussed the dependence of the CRI maps on the MR sequence and the estimated MR parameters. The maps also depend on parameters that are never measured, but are part of the CRI model. In the model proposed by Yarnykh, three a priori parameters are fixed and independent of the pulse sequence - the longitudinal and transverse relaxation times of the bound pool ($T_{1B}$ and $T_{2B}$), and the ratio of the transverse to longitudinal relaxation time of the free pool ($T_{2F}^T / T_{1F}^T$).

In order to determine the sensitivity of the CRI maps to the a priori parameters, we varied the parameters over their biologically plausible range ($T_{2B} = 7 – 13\mu s$, $T_{1B} = 0.3 – 2$ s, and $T_{2F}^T / T_{1F}^T = .03 – .07$) [12, 14,
For each combination of parameters we obtained unique k and BPF maps, and looked at their variation. Figure 11 shows that the BPF map is less sensitive to changes in the a priori parameters, as the k map tends to absorb most of the variation.

Figure 10: BPF sensitivity to the T1 parameter. (Top) T1 maps without (left) and with (right) B1 correction, resulting in a drift of the mean T1 value. Both maps are windowed to have the same contrast, but the colorbars show that the absolute values are different. (Bottom) The corresponding BPF maps show similar contrast, but the BPF maps with higher T1 values (right) have lower BPF values.

We tested the validity of the a priori parameters by calculating the mean RMS difference between the model fit and the data. While the quality of fit did not change dramatically with respect to the T1 and the T2/T1 parameters, it was sensitive to the T2B parameter. Figure 12 shows that for three different subjects the residual is minimized at different T2B values. This tends to indicate that T2B could be another free parameter in the CRI fits, but this would increase the complexity of the fitting, and (due to the non-linearity of the fit) it might degrade the quality of the CRI maps.

3. CRI INSIGHTS IN TISSUE MICROSTRUCTURE

In the previous section we outlined the challenges associated with obtaining precise and accurate CRI maps. Understanding these challenges is essential when considering potential applications of CRI in imaging tissue microstructure. Below we focus on two novel applications of CRI in imaging white matter in the brain, and cartilage in the knee, demonstrating the potential of combining CRI with more conventional imaging techniques.

Figure 11: Plot of the proportion change of BPF (left) and k values (right) when the a priori parameters are varied from one extreme to the other. The colormap shows that the k maps are more sensitive to the a priori parameters (hence the more intensive colors), and they also show more variability across tissues (hence the color non-uniformity).

Figure 12: Quality of fit plotted as a function of T2B. All three subjects have a U-shaped quality of fit curve, but the minimum varies across subjects. The optimal values tend to be around 8-9 μs. Also, white matter is better fitted compared to gray matter and has a slightly lower optimal T2B value. This could be due to the fact that white matter is better approximated by the Superlorentzian model.

3.1. CRI in the Human Brain

Diffusion tensor imaging (DTI) is currently the only method available to identify and measure white matter fascicles of the brain in vivo. The BPF was computed along brain fiber tracts obtained with DTI, and the fiber BPF score was used to identify clusters of fibers with high myelin content.

Figure 13 shows excellent reproducibility of the high BPF fibers across five healthy subjects. The anterior frontal callosal and superior longitudinal fasciculus groups are prominent in all subjects. Also, we see the optic radiation in all five subjects. While many fiber
The g-ratio is usually measured using myelin stains \textit{ex vivo}, and there is great interest in being able to map the g-ratio \textit{in vivo}. Figure 14 shows a simulated cross-section of the human corpus callosum, obtained by combining CRI and diffusion imaging. Estimates of the fiber volume fraction (FVF), myelin volume fraction (MVF) and the g-ratio were combined with published fiber caliber distributions to produce these cross-sections. While these results remain to be validated with histology, the obtained g-ratio values are within the range of values reported in literature [29].

3.2. CRI in the Human Knee

Cartilage damage in osteoarthritis is associated with loss of proteoglycan (PG) and degeneration of the collagen matrix. Biomarkers specific to macromolecular content (collagen or proteoglycan) may serve as an early indicator of osteoarthritis. Biochemistry measurements in articular cartilage show that the CRI parameters relate to collagen and proteoglycan concentrations in \textit{ex vivo} cartilage specimens [30].

Table 1 shows that unlike the more commonly used magnetization transfer ratio (MTR), the CRI parameters correlate with the biochemistry measurements of sulfated glycosaminoglycan (a measure of proteoglycan content) and hydroxyproline (a measure of collagen content) in cartilage plugs pulled from four \textit{ex vivo} cartilage specimens. The biochemistry amounts were normalized by water content.

The method remains to be explored \textit{in vivo}, but it is a promising new way of imaging cartilage that could be useful in early diagnosis of osteoarthritis.

### Table 1: Correlation of the CRI parameters with sGAG/WC and hydroxyproline/WC (reported in mg/ml) in articular cartilage for four \textit{ex vivo} cartilage specimens, reported as Pearson’s correlation coefficients. The statistical significance of each correlation is shown in parenthesis, and all correlations with $p < .05$ are shown in bold.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Patella 1</th>
<th>Patella 2</th>
<th>Patella 3</th>
<th>Tibia</th>
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<td></td>
<td></td>
<td></td>
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<td>-.12 (.69)</td>
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</tbody>
</table>

4. CONCLUSION

CRI provides useful biomarkers for studying areas with high macromolecular content, such as white matter in the brain and cartilage in the knee. The CRI maps are sensitive to different aspects of the MR pulse sequence, such as the $T_1$ mapping technique and the scanner drift. They also depend on several \textit{a priori} parameters, especially the transverse relaxation rate of the bound pool $T_2^B$. Proper understanding of the benefits and limitations of CRI imaging will open the way for novel imaging methods that provide insight in tissue microstructure.

5. REFERENCES


RADIATION DOSES IN COMPUTED TOMOGRAPHY IN SERBIA

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Abstract – There are 90 CT units operating in Serbia, with tenfold increase in the last decade, resulting with annual total of approximately 350,000 procedures. The objective of this paper is to assess typical patient dose from adult CT examinations. Initially, two hospitals with high workload were enrolled into the study. Both MDCT and SDCT were included, to represent typical practice. Typical patients exposure parameters based on predefined protocol for CT examinations of head, chest and abdomen were collected. Data were taken from CT unit display. This includes exposure parameters and CTDIvol. For MDCT DLP was also available on the display, while in case of SDCT the value was calculated from CTDI values and information on typical scan length. DLP values were 1020 mGy•cm, 590 mGy•cm and 890 mGy•cm for head, chest and abdomen respectively using SDCT and 1050 mGy•cm, 570 mGy•cm and 1000 mGy•cm for the same examination using MDCT. The assessed patients’ doses in terms of CTDIvol and DLP were below or slightly above the reference levels and in accordance with surveys from other countries, although the scope for dose reduction through optimisation of the examination protocol was observed.

Keywords – computed tomography, patient dose, CT dose index, dose length product

1. INTRODUCTION

Computed tomography (CT) is an evolving imaging modality and the most significant diagnostic examination from the radiation protection point of view. The frequency of CT examinations as well as individual dose per examination is increasing rapidly. CT can now be responsible for up to 17% of the departmental workload accounting for 70-75% of the collective dose from medical radiation [1]. The worldwide total number of CT examinations is estimated to 93 millions, corresponding to a frequency of 16 examinations per 1000 inhabitants, with about 11% involving children of age 0-15 [2,3]. The reported increase in request for paediatric CT range from 63% to 92% [1]. This figures reflect the very rapid technological development in CT imagining, i.e. introduction of single detector spiral CT units (SDCT) and multi detector units (MDCT) [4,5]. The number of detectors also affects the dose due to shape of the x-ray beam, referred as “overbeaming” [6,7]. The effect decreases with more detector rows and is less pronounced in 16- and 64-detector machines than 4- and 8-detector machines. Although there is remarkable variation in the number and properties of CT units and examinations increase of collective dose and dose per examination, both in adult and paediatric CT is a general trend [2].

There are 90 CT units operating in Serbia (more than ten 64-detector CT units), with tenfold increase in the last decade, resulting with annual total of approximately 350,000 procedures or 45 examinations per 1000 inhabitants. This number is continuously increasing. The frequency of paediatric examination is less than 1% due to technical reasons, but it is likely that number of paediatric examinations will increase in near future.

The objective of this paper is to assess typical patient dose from adult CT examinations. Initially, two hospitals with high workload were enrolled into the study.

2. MATERIALS AND METHODS

2.1. Dosimetry in computed tomography

There is currently much confusion on the use of dosimetric quantities in CT, which is partially driven by rapid development of the CT technologies [8]. Nevertheless, at present, the accepted dosimetry concept in CT is well established and based on the practical dose quantities: weighted CT dose index (CTDIw), volume weighted CT dose index (CTDIvol)
and dose-length product (DLP) [7-12]. With advent of MDCT, CTDIvol has become more relevant. As a quotient of CTDIw and pitch, it account for variation in radiation exposure in the z direction when pitch is not an unity. With use of a spiral SDCT, the CTDIvol is equal to CTDIw [4].

There are some shortcomings of using the CTDI, which is the most widely used quantity for CT dosimetry. This quantity is neither related to radiation risk not to noise level, since it is only an indication of average dose in the central part of scanned region when slices are contiguous [8]. It does not provide integral dose information, relevant for risk assessment and does not account for patient specific parameters. However, it enables comparisons between scanners, and can be easily measured. Another directly measurable quantity, DLP, is an indicator of overall radiation burden to patient [7]. Furthermore, CTDI and DLP are commonly used quantities to express Diagnostic Reference Levels (DRLs) in CT [11]. DRLs are an optimisation tool in patient protection and permit comparison of the performance of different CT scanners [4].

All CT vendors are now required to display CTDI or even DLP values on the user interface. However, these quantities do not tell anything about actual dose that patient receives. Instead, they are useful information about relative changes that result from alteration of examination parameters and tailoring examination to individual patient. It is worth mentioning that for a given set of parameters, displayed CTDI and DLP will be the same, regardless patient’s size, since these quantities do not reflect the absorbed dose to the body.

### 2.2. Data collection

The strategy for the present survey ideally involved the assessment of the CTDIvol and DLP for each sequence and examination. Basic parameters of the standard examination protocol for the commonly performed examinations in all radiology departments (head, chest and abdomen) were collected from the scanner display. Protocols suggested by the manufacturer were normally used. The method of data collection from displays was selected, since it has been shown that is sufficiently accurate in dose audit [10,13]. DLP was calculated from each sequence using information on the scan length.

Initially, two hospitals were involved in this preliminary survey. All hospitals have high workload. Both MDCT and SDCT adult examinations were included to represent typical practice.

SDCT (Somatom Plus 4, Siemens) is not equipped with automatic tube current modulation, while MDCT (BrightSpeed, General Electric) in another hospital has this option.

### 3. RESULTS

Typical examination protocol details for examination of head, chest and abdomen are presented in Table 1. These examination types were selected to cover a wide range of patient doses. The doses in term of CTDIvol and DLP are presented in Table 2.

**Table 1. Details on the typical CT scanning protocol for a given examination types in each hospital under the survey**

<table>
<thead>
<tr>
<th>CT model/ manufacturer</th>
<th>BrightSpeed/ General Electric</th>
<th>Somatom Plus 4/Siemens</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of detector rows</td>
<td>64</td>
<td>4</td>
</tr>
<tr>
<td>CT exam</td>
<td>head chest abdomen head chest abdomen</td>
<td></td>
</tr>
<tr>
<td>Tube potential [kV]</td>
<td>120 120 120 140 140 120</td>
<td></td>
</tr>
<tr>
<td>Tube loading [mA]</td>
<td>290 225 225 255 159 200</td>
<td></td>
</tr>
<tr>
<td>Slice width [mm]</td>
<td>5 5 5 5 5 5</td>
<td></td>
</tr>
<tr>
<td>Pitch</td>
<td>0.938 1.375 0.938 - - -</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CT model</th>
<th>BrightSpeed/ General Electric</th>
<th>Somatom Plus 4/Siemens</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT examination</td>
<td>head chest abdomen head chest abdomen</td>
<td>head chest abdomen</td>
</tr>
<tr>
<td>CTDIvol [mGy]</td>
<td>66 16 25 74 18 16</td>
<td>60 30 35 60 30 35</td>
</tr>
<tr>
<td>DLP [mGy cm]</td>
<td>1050 570 1000 1020 590 890</td>
<td>1050 650 780 1050 650 780</td>
</tr>
</tbody>
</table>

As an indication of an integral dose to patients, DLP values were 1020 mGy·cm, 590 mGy·cm and 890 mGy·cm for head, chest and abdomen CT respectively using SDCT and 1050 mGy·cm, 570 mGy·cm and 1000 mGy·cm for the same examination using MDCT.

Inherent differences in the design of CT equipment lead to large variations between scanner models in assessed dose for standard adult examination protocol and acceptable image quality. Spiral CT offers the ability to adjust the slice reconstruction interval. The use of higher pitch and tube current modulation are the major methods for balancing patient dose and image noise level, as presented in Table 1 and Table 2. The factors that affect the dose are scanner related, operator related or patient related. The first two are can be controlled either by manufacturers or by operators, while the last one cannot be easily controlled. However, the examination protocol must be related to the situation.
As presented in Table 2, the CT doses in terms of CTDI and DLP were below reference levels and in accordance with surveys from other countries [11,14-16]. Wide variation in doses indicates that there is a scope for dose reduction. Immediate action is possible by proper selection of the section thickness, increased scope for dose reduction. Immediate action is possible due to very limited sample, it is not possible to bring the general conclusion on the difference between SDCT and MDCT. Other survey results pointed out that these differences are significant and that DRRL should be set separately for these two technologies [10].

This survey is an initial input for assessment of CT doses in Serbia, since this issue has never been raised before. Standard examination protocols provide the basic framework for the typical practice, although the extended survey should be oriented towards individual patients in order to assess variation among them and towards establishment of national DRRL. This is especially relevant for further optimisation studies. In all hospitals enrolled into the survey the operators were not aware about magnitude of patients’ doses in CT and possibilities for dose reduction.

4. CONCLUSION

It is apparent that radiation protection issues in CT are extremely complex and they have become even more complicated with the introduction of MDCT. Commonly, radiologists are not aware about magnitude of patients’ doses in CT and possibilities for dose reduction. Protocol suggested by the manufacturer is normally used. As the number of units and examinations is increasing in Serbia, the training of operating staff is of utmost importance.

Extended survey should be performed on the national scale, resulting with setting of national DRRL. Also, the efforts should be made to train the operators and to increase their awareness about dose management and magnitude of patient doses in CT.

5. REFERENCES

MONITORING OF DOSES TO PATIENTS IN INTERVENTIONAL CARDIOLOGY: FIRST RESULTS FROM THREE SERBIAN HOSPITALS

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Abstract – The aim of this work is to assess level of radiation dose to patients in interventional cardiology procedures in three large Serbian hospitals and to investigate possibility for setting of trigger levels if dose quantities exceed certain levels. Three dedicated interventional cardiology laboratories were included in the survey. Information on annual workload was estimated based on number of coronary angiography (CA) procedures and percutaneous coronary interventions (PCI). Patients doses were assessed in terms of air kerma area product ($P_{KA}$) and air kerma in international reference point ($K_{IRP}$). Results were compared with internationally proposed Diagnostic Reference Levels (DRL) and similar surveys’ results.

Average total annual number of procedures was 820, 1100 and 2500 in three hospitals, respectively, while total number of dose measurements was 337. All three centers reported $P_{KA}$ values higher than 100 Gy·cm$^2$ and even values above 200 Gy·cm$^2$, corresponding to 42% and 16% of all measurements. Measured $K_{IRP}$ value higher than 5 Gy was reported in one center, indicating that skin doses associated possibility of skin injuries were observed. $P_{KA}$ mean hospital values for CA ranged from 33 to 78 Gy·cm$^2$ and for PCI from 73 to 113 Gy·cm$^2$, while associated values for $K_{IRP}$ were: 0.45-1.2 Gy and 1.1-1.8 Gy, respectively. Comparison of obtained results with international DRL indicated that significant number of procedures is not optimally performed as in some centers more than a half of patients receive doses above DRL. The presented results are valuable input for dose optimization strategies and increased awareness related to importance of dose management. With respect to high dose values, risk for stochastic effects and tissue reactions, dose management methods were proposed.

Keywords – interventional cardiology, dose, dose-area product, cumulative dose, interventional reference point

1. INTRODUCTION

Interventional cardiology procedures are classified as high-dose procedures [1], owing to increased risk for radiation skin injuries and stochastic effects, as cancer [2]. Numerous examples of deterministic effects (harmful tissue reactions) are described in literature [2-4], while associated dose levels can reach even 15 Gy during a single procedure [5]. Interventional cardiologists are one among most intensive users of x-rays. In spite of this, very often they are not aware of dose levels in interventional cardiology that are typically higher then in conventional radiology procedures. Patients undergoing interventional cardiology procedures are exposed to doses that are a few order of magnitudes higher than dose levels in conventional radiology. Furthermore, the number of interventional cardiology procedures is doubled every 2-4 years [4]. Therefore, application of radiation protection principles to protect patients and interventionalists is one of the most important challenges in interventional cardiology.

Dose levels in interventional cardiology procedures are such that allow for manifestation of deterministic effects (harmful tissue reactions) and stochastic effects [2, 6].

A particular challenge is the fact that the radiation damage of the skin is difficult to detect and connect to the previously conducted cardiologic procedures [4]. Dose received by patient, in general, depends on the radiological equipment, examination protocol, the way it is implemented and the patient's body weight and nature of disease. Long-term fluoroscopy of certain parts of the body, a significant body mass, high-value dose intensity, continuous rather than pulsed fluoroscopy, small focus-skin distance of the patient and repeated procedure on the same patient are among the factors that can lead to radiation skin injuries. In order to prevent these, a number of international organizations and professional bodies in their recommendations stated the importance of dose monitoring, or monitoring of other relevant
parameters that allow retrospective assessment of doses to patients [1, 2, 6-8].

Effective dose, as a measure of risk for stochastic effects can be estimated on the basis of Kerma – area product measurements (P KA), while Kerma on the surface of the skin of the patient as a measure of the risk of skin injuries (deterministic effects) can be measured using thermoluminescence dosimeters or films [3]. P KA is a measure of total energy of x-rays imparted in the patient. It can be relatively easily measured using a transmission ionization chamber without significant interference with examination protocol. Based on P KA value, the effective dose can be retrospectively estimated with reasonable accuracy, using a conversion factor of 0.18 mSv/Gy cm² [8]. P KA is an integral indicator of the duration of the procedure, its complexity, fluoroscopy modalities used and the number of acquisition series. However, P KA does not provide information on possible radiation injury of the skin, in particular, in interventional cardiology where a number of different projections is typically used. Given the practical limitations on usage thermoluminescence dosimeters or films, measurement of the air kerma in interventional reference point (K IRP) provides a reasonably good assessment of the risks for tissue reaction. By definition, the interventional reference point is the point at a distance of 15 cm from isocenter, towards x-ray tube [2]. K IRP is a conservative estimate of the dose to the skin surface, due to the cumulative effect of multiple views used during an examination. K IRP does not provide information on dose distribution to the patient's skin. In the absence of ideal dosimetry concept, both quantities, P KA and K IRP, together with the total fluoroscopy time are corsets for the determination of reference levels in interventional cardiology, primarily as an indicator of possible radiation injuries. In addition, noting these quantities as a part of each examination record is a requirement of the International Electrotechnical Commission (IEC) [2, 7].

Guidance levels (interchangeably used as reference levels or diagnostic reference levels) are therefore required in the International Atomic Energy Agency Basic Safety Standards as an important tool for optimization. They are an indication of “what is achievable with current good practice...”, but are “to be applied with flexibility to allow higher exposures if these are indicated by sound clinical judgment...” [8].

Guidance levels can be applied to practices both between and within hospitals. They may be used to identify practices in a hospital in which patient exposures are higher than the norm and hence where there is the greatest potential for dose reduction. Within a hospital, patient exposures may be monitored and guidance levels developed for specific interventions. This approach may be used to identify rooms where high exposure procedures are mostly performed. Optimization studies would then be concentrated on details regarding fluoroscopic equipment and practice [8].

However, the application of the reference levels concept is not straightforward in interventional cardiology, since the protocol is adjusted to individual characteristics of each patient [7-10]. Procedures can be very simple and very complex, a standard procedure can not be easily defined, as is the case in conventional radiology. One possible solution is implementation of a complexity index and definition of specific reference levels for different complexities of the same interventional cardiology procedures [8, 10].

The aim of this work is to assess level of radiation dose to patients in interventional cardiology procedures in three large Serbian hospitals and to investigate possibility for setting of trigger levels if dose quantities exceed certain levels.

2. MATERIALS AND METHODS

Three dedicated interventional cardiology laboratories were included in the survey. Information on annual workload was estimated based on number of coronary angiography (CA) procedures and percutaneous coronary interventions (PCI). Patients doses were assessed in terms of P KA and K IRP.

Therefore, the data were analyzed in terms of CA (the pure diagnostic procedure) and PCI. For the purposes of this study, PCI includes all forms of coronary artery interventions and may also include a partial or complete diagnostic study.

All cardiology procedures were performed at the x-ray unit of the same model: Siemens Axiom Artis (Siemens, Erlangen, Germany) with a flat panel detector and integrated in situ calibrated ionization chamber to measure the P KA. All x-ray units enrolled in the study are subject to regular testing and are equipped with all necessary protective tools.

Results were compared with internationally proposed Diagnostic Reference Levels (DRL) and similar surveys’ results.

3. RESULTS

Total annual number of procedures was 820, 1100 and 2500 in three hospitals, respectively, while total number of dose measurements was 337.

Results of P KA and K IRP measurements in three hospitals for CA and PCI are presented in Table 1 and Table 2, respectively.

All three centers reported P KA values higher than 100 Gy·cm² and even values above 200 Gy·cm², corresponding to 42% and 16% of all measurements (Figure 1). Measured K IRP value higher than 5 Gy was reported in one center (Figure 2), indicating that skin doses are associated with possibility of skin injuries were observed. P KA values for CA ranged from 36 to
78 Gy·cm² and for PCI from 73 to 142 Gy·cm², while associated values for KIRP were: 0.45-1.2 Gy and 1.1-2.2 Gy, respectively. Comparison of obtained results with international DRL for CA and PCI: 45 and 85 Gy·cm² for PKA and 0.65 and 1.5 Gy for KIRP, respectively, indicated that significant number of procedures is not optimally performed as in some centers more than a half of patients receive doses above DRL. As presented in Table 3, mean values of dose measurements in three hospitals from this study are in line with or slightly higher than other study results.

Table 1. Result of dose measurements for CA procedure in three hospitals. Corresponding mean values, standard deviation and range are presented.

<table>
<thead>
<tr>
<th>Hospital</th>
<th>Number of procedures</th>
<th>Age (y)</th>
<th>Fluoroscopy time (min)</th>
<th>PKA (Gy·cm²)</th>
<th>KIRP (Gy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>117</td>
<td>63 ± 13 (50-78)</td>
<td>8 ± 6 (0.2-52)</td>
<td>78 ± 70 (1-529)</td>
<td>1.2 ± 1.1 (0.10-6.7)</td>
</tr>
<tr>
<td>B</td>
<td>21</td>
<td>64 ± 9 (49-77)</td>
<td>7 ± 17 (1.1-80)</td>
<td>38 ± 17 (10-79)</td>
<td>0.45 ± 0.24 (0.14-0.98)</td>
</tr>
<tr>
<td>C</td>
<td>60</td>
<td>n/a</td>
<td>6 ± 3 (2.4-13)</td>
<td>33 ± 11 (10-49)</td>
<td>0.51 ± 0.27 (0.14-1.1)</td>
</tr>
</tbody>
</table>

Table 2. Result of dose measurements for PCI procedure in three hospitals. Corresponding mean values, standard deviation and range are presented.

<table>
<thead>
<tr>
<th>Hospital</th>
<th>Number of procedures</th>
<th>Age (y)</th>
<th>Fluoroscopy time (min)</th>
<th>PKA (Gy·cm²)</th>
<th>KIRP (Gy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>69</td>
<td>58 ± 9 (50-78)</td>
<td>11 ± 8 (0.2-43)</td>
<td>113 ± 82 (8-529)</td>
<td>1.8 ± 1.4 (0.10-8.7)</td>
</tr>
<tr>
<td>B</td>
<td>27</td>
<td>60 ± 10 (26-76)</td>
<td>15 ± 10 (3.0-50)</td>
<td>110 ± 79 (32-270)</td>
<td>1.5 ± 1.0 (0.32-3.6)</td>
</tr>
<tr>
<td>C</td>
<td>43</td>
<td>n/a</td>
<td>10 ± 6 (2.4-25)</td>
<td>73 ± 51 (10-245)</td>
<td>1.1 ± 0.8 (0.10-3.7)</td>
</tr>
</tbody>
</table>

Fig. 1 – Distribution of kerma area product values in interventional cardiology procedures in three hospitals

Fig. 2 – Distribution of cumulative dose to interventional reference point in interventional cardiology procedures in three hospitals

However, at the levels of individual hospital it is indicative that one hospital operates at higher dose levels compared to other hospitals and other studies’ results. Possible explanation is typically prolonged fluoroscopy time in this hospital (Table 1 and 2) and fact that large number of procedures is performed by junior cardiologists.
4. CONCLUSION

Based on the presented results and the associated risk for the patient, it is important and necessary to monitor dose to patient. This should become an integral part of the practice of interventional cardiology. Bearing in mind the availability of dosimetry data in electronic form, it is necessary that these values become part of patients’ medical record.

<table>
<thead>
<tr>
<th>Table 3. Comparison of dose measurements for CA and PCI (in terms of $P_{KA}$) to international DRL and results of other studies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>This work *</td>
</tr>
<tr>
<td>IAEA [8]**</td>
</tr>
<tr>
<td>Padovani et al. [10]</td>
</tr>
<tr>
<td>Brnić et al. [12]</td>
</tr>
<tr>
<td>UNSECAR*** [13]</td>
</tr>
<tr>
<td>NCRP [14]</td>
</tr>
<tr>
<td>Neofotistou et al [15]**</td>
</tr>
</tbody>
</table>

* mean from 3 hospitals  
**DRL also given in terms of fluoroscopy time  
***reported range based on 34 literature sources

Patient should be informed about possible skin effects, if dose level is higher then trigger. In addition, it is recommended to perform more specific dose studies using radiochromic films occasionally [3, 7, 10]. Most radiation injuries, especially those serious could be avoided if radiation protection measures are applied and if staff is regularly trained and if cardiologists use the equipment properly. This includes: use of appropriate filtration, the application of pulse fluoroscopy, appropriate solutions for compensation for various attenuation properties of different body parts, careful use of beam angulations, reducing the patient-to-focus distance, avoiding repeat procedures in the same patient and regular training of the operators [11].

It is very important to organize appropriate training activities contributing to physician awareness in the use of radiation, as there are proofs of and there was a statistically significant reduction in patient exposure after these dedicated training activities [8]. Another important training consideration is the existence of a national or local requirement for interventional cardiologists.

The presented results are valuable input for dose optimization strategies and for increasing awareness related to importance of dose management in interventional cardiology.

5. REFERENCES


TESTING THE NEW AAPM FORMALISM FOR THE EVALUATION OF RADIATION DOSE IN X-RAY COMPUTED TOMOGRAPHY

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Abstract – A standardized way to characterize the radiation dose in computed tomography (CT) is to measure the Computed Tomography Dose Index (CTDI). There are several definitions of CTDI which appeared during the course of the CT development. AAPM has recently issued a report no. 96 dealing with the measurement, reporting and management of the radiation dose in CT. But during the last decade negative sides of CTDI appeared and in February 2010 AAPM issued another protocol for stating and measuring the radiation dose in CT, quite different from the previous one. In this work we compare measurements in air with two different protocols, one of the IAEA (Technical Report Series no. 457) and the other protocol based on the AAPM report no. 111. The dose difference on the central CT axis between the measurements with these protocols was less than 2%. Also, the peripheral doses in the field of view were in the uncertainty boundaries characteristic for dosimetric measurements in diagnostic radiology. The AAPM report no. 111 replaces the longtime used CTDI formalism with the one in which measurement of equilibrium dose-pitch product can be obtained with a Farmer type ionization chamber. The new measurement formalism can be used to state the radiation output of a CT unit as well as to predict some future malfunction of that unit.

Keywords – CTDI, Computed Tomography,

1. INTRODUCTION

It is a common knowledge amongst radiologists and medical physicist that the computed tomography (CT) contributes to nearly 70% of the total dose given to patients during diagnostic examinations in the developed countries. This trend is expected to grow worldwide as the number of installed CT machines, and in the same time CT examinations, in the world grows from year by year. That fact requires the measurement of the radiation dose delivered from CT scanners to be precise and unambiguous. Today, a standardized way to characterize the radiation output in computed tomography is to measure the Computed Tomography Dose Index (CTDI). Basically, it represents the integrated dose along the z axis (the axis perpendicular to the imaging plane) from one axial CT scan. Several definitions of CTDI have been derived in order to facilitate dose description from the CT radiation. Despite that, the CTDI is difficult to interpret especially with the new generations of Multiple Detector-Row CTs [1]. This is primarily because the CTDI was defined for axial scanning in scanners with one row of detectors. Now, the new generations of scanners all perform helical scanning with several slices taken in the same time.

This work aims to compare the results of the measurements free-in-air with a pencil chamber specially designed for CTDI measurements and a conventional Farmer type ionization chamber. The international dosimetry protocols allow measurements free-in-air and then converting the results to dose to a phantom. The free-in-air measurements are straightforward and allow a direct comparison of the results. Being comparison measurements, the described procedure is actually performance of relative dosimetry.

2. MATERIALS AND METHODS

All measurements were done on a GE HighSpeed scanner we use for radiotherapy simulation purposes. This scanner is one-row detector scanner with a helical scanning capability. Classical way of CTDI measurement was performed with Barracuda system product of RTI Electronics AB. The new measurement paradigm was performed with PTW UNIDOS electrometer with Farmer type ionization chamber TW30013.
The CT-SD16 semiconductor pencil detector was used as a detector during the classical measurement that was performed free in air. This detector is designed with the helical scanning in mind and because of that its preferable use is for helical scanning measurements. The conditions of irradiation were identical in both cases and derived from the AAPM report no. 111 [2]. According to this recommendation the scan length was 8 cm with 4 cm longitudinally on each side of the center of the detectors. The chambers were positioned in a way as to minimize the scatter radiation from the table. The measurements were made with detectors centered on the axis of the CT tube rotation as well as the in two lateral, left and right, positions 7 cm off the center under the angle of 45° above the frontal plane. These lateral positions mimic the measurement in a head phantom in the peripheral upper holes of the phantom. During the scanning the movement of the detectors was perpendicular to the imaging plane. The positioning of the detectors was made with the help of the LAP lasers which determine the isocenter of the imaging plane. Their accuracy positioning is better than 2 mm.

The scanning was made in a helical mode with tube rotation time of 2s and slice width of 1 cm. The tube voltage was selected to be 120 kV with a 200 mA tube current. The pitch factor was taken to be 1. The scanning was chosen to be in the head field of view mode.

The IAEA international protocol [5] requires the CTDI measurements to be made in air as well as in a plastic head or/and body phantoms. In that way the CTDIw can be calculated and it is the parameter that is usually stated on the CT unit console.

According to the AAPM Report No. 111 [2] there is no consensus about what type of phantom should be used for the CTDI determination. This is a new formalism and there in no commercially available phantoms suitable for the CTDI measurements. Despite the fact that the phantom geometry is not crucial for the measurements, it involves additional uncertainties when converting the measurements in one phantom to the values of CTDI for other phantom. Because of that, the easiest way for comparing measurement results is to measure the dose (or air kerma) in air. One thing that facilitates getting accurate results is the fact that for the energy range in the CT scanning (120 kV) an electronic equilibrium is established in the Farmer type chamber.

3. RESULTS

The measurement with the CT-SD16 detector gave dose values of 86.6 mGy on the central axis while the average result of the measurements with the PTW TW30013 chamber was 85.0 mGy. Relative uncertainty of less than 2% enters the boundaries of measurement errors. These values are equivalent to the CTDI_{air} concept. On the other side, this concept is equivalent to $\hat{D}_{eq,air}$ - equilibrium dose-pitch product (mGy) for air as defined in reference [2]. The air kerma profile for the geometry depicted previously is shown in Fig.1.

Additional free-in-air measurements were made in positions where would have been found the holes of a head phantom. Two upper positions of 'would be holes' were only tested. They are positioned 5 cm above the frontal plane and 5 cm left and right of the sagittal plane. It can be seen that only the measurements in the upper right position show significant difference between the two types of measurements (11.2%). We treat the measurements with the ionization farmer type of chamber as a more stable measurement and, more important, uninfluenced by the field of view.

In a similar work [4] the authors have made cross comparison of pencil chambers and Farmer type chambers by making free-in-air measurements. Their work showed excellent equivalence of the two types of measurements. When the measurements are normalized to a pitch factor equal to 1, the results of measurements are almost identical. When the measurements in air are reliable, the conversion to phantom or tissue doses is much easier.

In Tab. 1 the results of the measurements with two apparatus are shown. We explain the higher difference of the results in the upper right position measurements with the higher sensitivity of the CD-SD16 detector and related software to small positional inaccuracies. An accurate positioning free-in-air of the detectors in peripheral positions is very difficult without the help of external lasers as used for radiotherapy simulations. In the IAEA protocol, in the code of practice for clinical measurements, uncertainties of 6.3% (one standard deviation) are considered acceptable for measurements in the diagnostic radiology. So, our relative error of max 6.1% is well in tolerance boundaries for measurements in clinical conditions.

Fig. 1 – Dose profile free-in-air measured with pencil chamber

In Tab. 1 the results of the measurements with two apparatus are shown. We explain the higher difference of the results in the upper right position measurements with the higher sensitivity of the CD-SD16 detector and related software to small positional inaccuracies. An accurate positioning free-in-air of the detectors in peripheral positions is very difficult without the help of external lasers as used for radiotherapy simulations. In the IAEA protocol, in the code of practice for clinical measurements, uncertainties of 6.3% (one standard deviation) are considered acceptable for measurements in the diagnostic radiology. So, our relative error of max 6.1% is well in tolerance boundaries for measurements in clinical conditions.
One of the first theoretical expositions of the CD dose measurement with small ionization chamber was done in reference [3]. An experimental setup with a small chamber was also described there and the obtained results were compared to the measurements with a pencil detector. An inadequacy of a long pencil chamber for measurements in phantoms was demonstrated yielding up to 10% smaller dose for one-slice axial scanning.

Table 1. Measurements free-in-air with two types of detectors

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4. CONCLUSION

With the advent of the new highly sophisticated CT units (Multi Detector Cone Beam Computed Tomography) the measurement of their radiation output changed the meaning from the old one. The CTDI concept proved to be cumbersome in new situations and a new measurement paradigm has appeared. In this work a simple measurement is performed which shows that CT radiation output can be quantified in an easier way with a conventional Farmer type ionization chamber. The results of the measurements can be used both to state the radiation output of the CT unit and also to predict any malfunction of that unit.

5. REFERENCES


OPTIMIZATION OF RADIATION PROTECTION (ORP) OF WORKERS IN NUCLEAR MEDICINE DEPARTMENT OCCUPATIONALLY EXPOSED TO IONIZING RADIATION

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Abstract – Occupational radiation exposure of nuclear medicine personnel arise either from external irradiation during the handling or from the entry of radioactive substances in the body; the major source of external irradiation is the patient that has received a radiopharmaceutical for diagnostic or therapeutic purposes. In this study we present the dosimetry monitoring of the personnel at the Institute of Pathophysiology and Nuclear Medicine in Skopje (IPNM) before and after the implementation the methods of ORP.

Twenty-seven employees were optimized with standard TLD card, monthly, expressed as whole body personal dose in the period of use of dosimeter. Annual Effective Doses (AED) are presented for years: 2001, 2004, 2005, 2006, 2007, 2008. In the year 2005, after measurement from Technical Service Organization, IPNM Radiation Protection Officer (RPO) designed and implemented new recommendation and modality such as: designation of areas, introducing ambiental dose measurements, classification of employees, personnel rotation, risk assessment, occupational dose constraints, education of personnel, compliance with written procedures and establishing the Programme for Radiation Protection (RP). ORP measures were applied during the year of 2006, so the results of 2001, 2004 and 2005 correspond to unoptimized RP.

We were evaluated three groups: radiopharmacy laboratory (RPL), nuclear medicine technologist (NMT) and medical doctors. The third group was further divided according to the AED in the NMT group with AED below 1.6 mSv (MD1), and group with AED above this level (MD2). The average AED in the NMT group for 2005 was 3.59 mSv, while in 2008 it was 1.8 mSv; for MD1 group in 2005 was 1.5 mSv and in MD2 was 3.0 mSv. The average AED in 2008 for MD1 was 1.1 mSv, while MD2 group comprised of only one subject with annual effective dose of 1.76 mSv. The most exposed groups were nuclear medicine technologists (NMT) and medical doctors routinely involved in everyday nuclear medicine procedures (MD2).

The results from our study clearly show the reduction of external radiation dose at the IPNM after establishment of ORP measures in 2006. The reduction was most significant in the groups that had the highest radiation burden.

Keywords – radiation protection, dosimetry, optimization, ALARA

1. INTRODUCTION

Occupational radiation exposure of nuclear medicine personnel arise either from external irradiation during the handling of unsealed radioactive sources and radioactive patients, or from the entry of radioactive substances in the body. In nuclear medicine the major source of external irradiation is the patient that has received a radiopharmaceutical for diagnostic or therapeutic purposes. Contamination from unsealed radioactive substances may produce further external irradiation hazard.

In this study we present the dosimetry monitoring of the personnel at the IPNM before and after the implementation the methods of ORP.

2. MATERIALS AND METHODS

2.1. Personal dosimetry monitoring

Under the personal dosimetry monitoring are approximately 45 employees of the IPNM per year, but RP of only 27 employees was decided to be optimized and only they were included in this study. Standard TLD’s (TLD card with two elements of LiF -Harshaw/Bicron TLD 100) were carried monthly and the readings were performed by the Laboratory for Radiation Dosimetry at the Institute of Public Health of Republic of Macedonia. The measurements and readings are based on documents: IEC 1066 [1], IAEA RS-G-13 [2], ICRP 75 [3] and National Law on radiation safety [4].
These readings are expressed as whole body personal dose equivalent Hp(10) substracted by value of background measured in the period of use of dosimeter. From these readings AED was calculated for every employee within the study and doses less than 0.1 mSv are registered as 0.09 mSv.


2.2. Technical Service Organization (TSO)
At the end of 2005 TSO was invited to conduct variety of dosimetry measurements at the IPNM. Ambiental as well as workingplace monitoring comprised all affected areas: radiopharmacy laboratory (radioisotope Mo/Tc-generator, production of radiopharmaceuticals, compound labeling, QC of radiopharmaceuticals), gamma-camera scan rooms, low energy and high energy radioisotopes storage space, low energy and high energy radioisotopes application labs, temporary radioactive waste storage etc. The appropriate report was issued by the TSO afterward, and as a result of mutual analysis and agreement between TSO and IPNM RPO, recommendations for ORP were produced.

2.3. Optimization of Radiation Protection
Recommendations and the method of ORP comprised:
- designation of areas,
- introducing ambiental dose measurements,
- classification of employees,
- personnel rotation,
- risk assessment,
- occupational dose constraints,
- education of personnel,
- compliance with written procedures and
- establishing the Programme for RP.

The beginning of 2006 was starting point for implementation the variety of modalities of the ORP.

All affected areas with ionizing radiation were designated and marked with appropriate radioactive warning signs. Radioactive patient room was rebuild and shielded by lead foil. Monthly ambiental TL dosimetry was introduced in 8 different laboratories of interest. Classification of employees as class A an B workers was done. All gamma-camera technologists became a part of rotation schedule working plan; everyone was to spend one month at one gamma-camera i. e. four weeks in morning and afternoon shifts, one by another respectively. After one month everyone was to change the next gamma camera in the same manner. Working habits and acting of the employees were changing towards full compliance with written procedures. Two and half months education course in the field of basic nuclear physics, interaction of ionizing radiation and matter, detectors, planar, SPECT and PET gamma-camera systems, computers in NM, radiation dosimetry and protection has been performed, exams taken and local recognition diploma issued. Programme for Radiation Protection was established, elaborated and written, and at that time became only official document of a kind in the country.

3. RESULTS
The results from the monitored personell were evaluated in groups according to the working place and duties. The first group (RPL) comprised of personell in the radiopharmacy involved in the preparation and labeling of the radiopharmaceuticals, second group were nuclear medicine technologist (NMT) and the third group were medical doctors and physicists. The third group was further divided according to the AED in group with AED bellow 1.6 mSv (MD1), and group with AED above this level (MD2).

ORP measures were applied during the year of 2006, so the results of 2001, 2004 and 2005 correspond to unopimized RP, and the results of 2006, 2007 and 2008 give a picture of optimized RP.

The overall average annual effective dose (OAED) for all employees showed significant decrease after the introduction of ORP measures. The average OAED for the three years before the ORP was 2.1 mSv, while after the ORP the average for the years 2006-2008 was 1.5 mSv. In view of this results it should be taken in consideration that the average OAED for 2006 when the ORP programme started was 2.0 mSv, while two years later when the practice of ORP was steadily established the OAED was 1.1 mSv.

The most exposed groups to external irradiation were the groups of nuclear medicine technologists (NMT) and the group of medical doctors routinely involved in everyday nuclear medicine procedures (MD2). These groups are the one that show the most significant decrease in AED in years 2007 and 2008. The results for all four groups in the years before and after the introduction of ORP are shown in the Figures 1-6.

The average AED in the NMR group for 2005 was 3.59 mSv, while in 2008 it was 1.8 mSv. The average AED in MD1 group in 2005 was 1.5 mSv and in MD2 was 3.0 mSv. The average AED in 2008 for MD1 was 1.1 mSv, while MD2 group comprised of only one subject with annual effective dose of 1.76 mSv.

4. CONCLUSION
The results from our study clearly show the reduction of external radiation dose at the IPNM after establishment of ORP measures in 2006. The reduction was most significant in the groups that had the highest radiation burden.

The handling of radioactive sources and radioactive patients in nuclear medicine departments should be done according to recommended procedures by the national and local radiation safety law and rules to minimize the occupational radiation exposure of employees and to bring up the occupational radiation protection to higher level, taking into account the basic principles of ALARA philosophy: justification, limitation and optimization.
5. REFERENCES

[1] IEC 1066: Thermoluminescence dosimetry systems for personal and environmental monitoring; 2006


EFFECTIVE DOSES TO FAMILY MEMBERS OF PATIENTS TREATED WITH RADIOIODINE 131

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Abstract – Purpose: The purpose of this study was to evaluate the effective dose to family members of thyroid cancer and hyperthyroid patients treated with radioiodine 131; also to compare the results with dose constraints proposed by International Commission of Radiological Protection (ICRP) and Basic Safety Standards (BSS) of the International Atomic Energy Agency (IAEA).

Material and methods: for estimation of effective doses at sixty family members of thirty thyroid cancer and thirty hyperthyroid patients treated with radioiodine 131, the thermoluminiscent dosimeters, Model TLD 100, were used. Thyroid cancer patients were hospitalized for three days, while hyperthyroid patients were treated on out-patient basis. The family members wore thermoluminiscent dosimeter in front of the torso for seven days.

Results: The radiation doses to family members of thyroid cancer patients were well below recommended dose constraint of 1 mSv. The mean value of effective dose was 0.21 mSv (min 0.02 - max 0.51 mSv). Effective doses, higher than 1 mSv, were detected at 11 family members of hyperthyroid patients. The mean value of effective dose at family members of hyperthyroid patients was 0.87 mSv (min 0.12 - max 6.79)

Conclusion: After three days of hospitalization and detailed given oral and written instruction, thyroid carcinoma patients maintain not to exceed the proposed dose limits. Hyperthyroid patients present a greater radiation hazard than thyroid carcinoma patients. The estimated effective doses were higher than the effective doses at family members of thyroid carcinoma patients. These findings may be considered when establishing new national guidelines concerning radiation protection and release of patients after a treatment with radioiodine therapy.

Keywords – radioiodine 131, effective dose, TLD, relatives

1. INTRODUCTION

Many types of cancer and some other non-malignant diseases can be treated with radiations emitted by radionuclides. The unsealed radionuclides, that are injected, ingested, or inhaled, and which move through the body, are radiopharmaceuticals. This can localize in body tissues until they decay or they can be eliminated through various pathways, such as sweat and saliva and excreted into urine and feces. The radionuclides used for radiopharmaceutical therapy are usually relatively short-lived beta emitters. Most of these radionuclides also emit photons, which usually contribute minimally to the treatment dose, but produce an undesirable radiation field emanating from the patient. The most frequently used radiopharmaceutical for treatment of thyroid diseases, such as Thyroid Cancer and Hyperthyroidism, is the radioactive iodine 131. It has very high success rate in treatment of patients with thyroid diseases and it has also proven to be safe and a relatively inexpensive treatment modality. The treatment renders the patient radioactive. The patients, treated with radioactive iodine 131 present a radiation hazard to other individuals such as hospital staff, the patient’s family and members of the public with whom a treated patient may come in close contact. This situation can be overcome by imposing restriction on the behavior of the patient, to minimize the dose to close relatives and other individuals. In 1991, the International Commission of Radiological Protection (ICRP) [1] has recommended a radiation constraint of 1 mSv/year to the general population.
According to Basic Safety Standards Directive [2], the dose limits to the general public are not valid for “exposure of individuals, who are knowingly and willingly helping, other than as part of their occupation, in the support and comfort of in-patient and our-patients undergoing medical diagnosis or treatment”. Proposed dose constraint from the BSS is: 0.3 mSv per episode for public, 1 mSv for children, for the adults up to sixty years the dose constraint is 3 mSv and for adults more than 60 years old it is 15 mSv. The implementation of this guideline differs among various countries. In the Republic of Macedonia about 50 thyroid cancer patients are treated on in-patient basis and approximately the same number of hyperthyroid patients is treated ambulatory on out-patient basis. According to the local hospital rule and the old guidelines, the maximum given activity to hyperthyroid patients, treated on out-patients basis, is 1110 MBq. The new, not yet established guidelines, proposed to reduce the maximum given activity to hyperthyroid patients, treated on out-patient basis, from 1110 MBq to 555 MBq. This group of patients presents great radiation hazard to their family members. Upon discharge from hospital, the patients as well as their family members were given brief radiation safety instructions. The aim is to minimize the transfer of radioactive material to persons coming in close contact with the patient. There are several papers in the literature concerning the subject of doses received by family members of thyroid cancer and hyperthyroid patients [3-8]. Most of the published studies agree that doses to the family members are bellow the proposed dose constraint of 1 mSv. But there are also several papers [5, 9] that present cases where children or other persons have received higher radiation doses than proposed dose limit and usually it is case with hyperthyroid patients and their relatives. This study was undertaken to measure the effective doses to family members of patients treated with radioiodine 131 for thyroid diseases at our nuclear medicine centre.

2. PURPOSE

The main purpose of this study was to estimate the radiation exposure to family members of patients treated with radioiodine 131 either for thyroid carcinoma or hyperthyroidism. The other purpose was to use the results to identify necessary restrictions to ensure recommended dose constraint proposed by ICRP and BSS from the IAEA.

3. MATERIALS AND METHODS

The study population comprised thirty family members of the same number of thyroid cancer patients and thirty family members of thirty hyperthyroid patients. The total number of people included in the study was hundred and twenty. The administered dose for treatment of Thyroid cancer patients ranged from 3700 MBq to 5550 MBq of 131I. Mean administered dose was 3539 MBq. Twenty six patients received 3700 MBq, two patients received 4440 MBq and two patients received 5550 MBq radioiodine 131. They were hospitalized three days after administration and the dose rate was measured every day at distance of 0.25 m, 0.5 m, 1.0 m and 2.0 m by medical physicist. The dose rate measurements were performed with calibrated survey meter “mini-rad” series 1000, Morgan. When the level of 8 µSv/h at 2m was reached the patients were released from hospital. Upon discharge, the patients were given radiation safety instructions for their further behavior, in order to minimize the transfer of radiation to persons coming in close contact with them, especially children and pregnant women. Their relatives wore the TLD for one week and they were informed not to stay very close to the patient; and if so, to reduce the time of staying. It was suggested to maintain the distance between them and patient more than 2.0 m and to reduce time of staying less than 10 minutes up to one hour. Hyperthyroid patients were treated with 185 MBq to 1295 MBq of radioiodine 131. Mean administered dose activity was 683 MBq. Ten patients were diagnosed with Autonomous adenoma, eight with hyperthyroidism, six with Struma Diffuse Toxic, two with Struma Nodular Toxic and one patient was follow up with Ca. papillarae as well as one patient with Morbus Basedow syndrome. External dose rate measurements were performed at the same distance as Thyroid cancer patients fifteen minute after administration of therapy. After that they were released from hospital. The patients were interviewed and informed on the research aims by medical physicist and physician. They signed an agreement for receiving a therapy and all patients and their relatives feel positive about participating in the study. Family members groups were consisted of 12 female and 18 male person in the hyperthyroid group and 24 male and 6 female in the thyroid cancer group. Their age varied from 15 up to 80 years. The effective dose measurements were done with thermoluminescent dosimeters, model TLD 100, which contains hot pressed chips from lithium fluoride (LiF:Mg,Ti) with 3 mm² square, encapsulated between two sheets of Teflon 10 mg/cm² thick and mounted on an aluminium substrate with-bar code and within shielded filter holders (type 8814 Harshaw). A detection threshold of a dosimetry system is 0.0054 mSv. TLD’s were most appropriate to estimate radiation because the amount of ionizing radiation is directly proportional to the effective dose [10]. Actually it was estimated Hp (10). These types of dosimeters have photon energy response for gamma rays that ranges from (15 keV- 3MeV) (IEC 1066). The TLD Reader and Cards are calibrating on regular basis. The combined standard uncertainty of a dosimetry system is less than 15%. The control TLD was kept separately to measure the background. The background readings were subtracted from the readings of estimated effective doses to relatives TLD’s.
4. RESULTS AND DISCUSSION

4.1. Thyroid cancer patients

Table 1 presents the effective dose to relatives of the thyroid cancer patients treated with radioiodine 131, measured by TLD dosimeters. They have worn the TLD for one week. The sum of the effective dose varied from 0.02 mSv to 0.51 mSv. At three family members the TLD showed value 0 mSv and the explanation was that patients continue to be isolated from others after they had left the hospital for one week period of time.

Table 1. Effective doses to family members of Thyroid cancer patients

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Mean 0.21

The mean value of the effective dose to spouses of thyroid cancer patients is 0.21 mSv.

The figure 1 presents the effective doses to relatives of thyroid cancer patients treated with radioiodine 131 as measured by TLD dosimeter. They have worn the TLD for one week period. The figure 1 presents the effective doses to relatives of thyroid cancer patients versus proposed dose constraint for adults of 3 mSv and 15 mSv for older than 60 years according BSS. All values, except one, are below 3 mSv. The results presented in this study confirm the results of the other studies by Culver et al., stating that the doses for relatives of hyperthyroid patients are higher than the doses for relatives of thyroid cancer patients. This observation is due to the lower retention and the faster wash – out of the iodine 131 activity from the body of the thyroid carcinoma patients, in spite of the used in performing radioiodine therapy for thyroid cancer patient is done on safety way. Three days of hospitalization and dose rate measurements should be continued. It is recommended to install an additional seven days of sleeping separately and avoiding close contact to other people, children and pregnant women [11]. Giving written instructions on the further behavior of the patients at home will improve a process of optimization in radiation protection to family members, public and environment. Mathieu et al. reported the dose to family members and children of thyroid cancer patients, and in all cases the measured doses were lower than 0.5 mSv [6].

4.2. Hyperthyroid patients

Table 2 presents the effective doses to relatives of the hyperthyroid patients treated with radioiodine 131 as measured by TLD dosimeter. They have worn the TLD for one week period.

There were 12 female and 18 male relatives. The mean value of the effective dose for the relatives of the hyperthyroid patients was 0.87 mSv. The range of the effective dose varied from 0.12 mSv to 6.79 mSv. At three patients spouses were measured value 0 mSv, and the explanation was that the patients stayed in different room and most of the time were away from home. Only the spouse of patient number 18 received the highest remarkable dose with value 6.79 mSv. The explanation was that the woman did not follow the given recommendation. She stayed very close to her husband all the time after he received the therapy. With further analysis, we found that it was woman aged 69 and according to BSS for the adults aged more than 60 years the allowed dose constraint is 15 mSv. Eleven family members received effective doses higher than 1 mSv but less than 3 mSv.

On the figure 2 are presented the values gained from all hyperthyroid patients vs. Dose Constraint from the BSS. All values, except one, are below 3 mSv. The results presented in this study confirm the results of the other studies by Culver et al., stating that the doses for relatives of hyperthyroid patients are higher than the doses for relatives of thyroid cancer patients. This observation is due to the lower retention and the faster wash – out of the iodine 131 activity from the body of the thyroid carcinoma patients, in spite of the
higher administered activity. The hyperthyroid patients were treated on out-patient basis. The thyroid cancer patients after received activity were hospitalized for three days in an isolation room. That is one of the explanations for the higher doses to family members of hyperthyroid patients. The other reason for the differences of the effective doses to family members is that thyroid cancer patients retain less iodine as a result of the minimal thyroid tissue left after surgery. The given oral and written instructions were same, either for hyperthyroid or thyroid cancer patients. The restriction time is different (seven days for thyroid cancer patients and three days for hyperthyroid patients) and this information is usually given orally by the physicians. Even the radiation doses to hyperthyroid family members are within recommended limit; the values are higher in comparison with the doses of family members from thyroid cancer patients. Although the recommended dose limits are generally well met among the family members of thyroid cancer patients as well as hyperthyroid patients, the higher doses of the last one are related to higher 131I retention by the gland and justify more extended and stringent restriction periods [6].

Table 2. Effective doses to family members of Hyperthyroid patients

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<td>80</td>
</tr>
<tr>
<td>12</td>
<td>0.54</td>
<td>m</td>
<td>40</td>
</tr>
<tr>
<td>13</td>
<td>0.17</td>
<td>m</td>
<td>32</td>
</tr>
<tr>
<td>14</td>
<td>0.16</td>
<td>m</td>
<td>56</td>
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<td>16</td>
<td>1.90</td>
<td>m</td>
<td>55</td>
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<tr>
<td>17</td>
<td>0.33</td>
<td>f</td>
<td>52</td>
</tr>
<tr>
<td>18</td>
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</tr>
<tr>
<td>19</td>
<td>0.21</td>
<td>m</td>
<td>56</td>
</tr>
<tr>
<td>20</td>
<td>1.23</td>
<td>m</td>
<td>66</td>
</tr>
<tr>
<td>21</td>
<td>0.38</td>
<td>f</td>
<td>33</td>
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<tr>
<td>22</td>
<td>0.40</td>
<td>f</td>
<td>44</td>
</tr>
<tr>
<td>23</td>
<td>0.21</td>
<td>m</td>
<td>57</td>
</tr>
<tr>
<td>24</td>
<td>0.00</td>
<td>m</td>
<td>40</td>
</tr>
<tr>
<td>25</td>
<td>0.51</td>
<td>f</td>
<td>43</td>
</tr>
<tr>
<td>26</td>
<td>1.25</td>
<td>f</td>
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<td>1.48</td>
<td>f</td>
<td>50</td>
</tr>
<tr>
<td>28</td>
<td>1.32</td>
<td>f</td>
<td>42</td>
</tr>
<tr>
<td>29</td>
<td>1.70</td>
<td>f</td>
<td>47</td>
</tr>
<tr>
<td>30</td>
<td>1.17</td>
<td>f</td>
<td>60</td>
</tr>
<tr>
<td>Mean</td>
<td>0.87</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 2. Effective doses to relatives of Thyroid cancer patients vs. Dose Constraint of 15 mSv and 3 mSv

5. CONCLUSION

The radiation doses to family members of patients treated with radiiodine 131 for Thyroid cancer were found to be well below proposed dose limit of 1 mSv. Thyroid cancer patients should continue to be treated as in – patient to be sure that after three days of hospitalization they do not present radiation hazard to their family members.

The effective doses at eleven family members of the hyperthyroid patients were higher than 1 mSv. One person received 6.79 mSv.

It is necessary to formulate new guidelines on the instructions of out-patients after treatment with radiiodine 131 to comply with requirements based on the revised ICRP limits.

This study has provided useful information on radiation protection and exposure to family members of patients with Thyroid carcinoma and hyperthyroid patients treated with radiiodine 131.

Acknowledgements. This study was supported by the colleagues from the Public Health Institute, Skopje, Republic of Macedonia, where the analysis of TLD’s was carried out.

6. REFERENCES


DOSIMETRY TREATMENT PLANNING WITH UNCERTAINTY EVALUATION

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Abstract – Purpose/Objective: Treatment planning results can be presented as a dosimetry report, consisting of a number of images, curves, indices, etc. and in a prescription for the delivery of the planned treatment. A complex decision process is needed in order to decide which the optimal plan is. Since this decision is based on dose computations with their associated uncertainty, a modern treatment planning process has to deal with the effects of uncertainty to achieve maximum accuracy. Several tools are presented allowing the user to work with uncertainty. Modified dose volume histograms can help evaluate competing plans so that a proper hierarchy can be established amongst different goals.

Material/Methods: A central estimate of a dose volume histogram curve and two limit curves define an “indifference” band in the dose volume plane. Every plan within this band can be considered not better than the initial one, because uncertainty does not allow telling them apart. If a DVH goal is met within the indifference band, the user can aim to improve a different goal.

Results: The methods proposed in this work are easily introduced in clinical practice. They are compatible with an iterative optimization process adding few steps to the computation.

Conclusion: Accuracy requirements in radiation therapy keep on increasing, while accuracy in dose measurement or modeling is only moderately improving. Although it is a minor part in the overall uncertainty budget for the treatment, computation uncertainty affects decision making. Our method help make decisions with a maximum of information. This novel method can also provide quantitative measures of the probability of achieving the goals.

Keywords – Treatment planning, Dose volume histogram, Expectation value.

1. INTRODUCTION

Dose expected-volume histograms (DeVH) were introduced to help take into account absorbed dose computation uncertainty in planning evaluation [1]. According to the results obtained when modeling the treatment beam, a measure of uncertainty (standard deviation) can be derived, and used for DeVH computation. DeVH were shown not to be sensitive to the choice of uncertainty [2]. A series of new tools have been developed along with DeVH, particularly alpha-dose volume histograms (α-DVH) that help define confidence intervals for DeVH and DVH.

New criteria for decision making when uncertainty is taken into account are needed, and some evaluations have to be based on fuzzy logic instead of deterministic considerations. In addition, optimization routines can be modified in order to work with these new tools.

2. MATERIALS AND METHODS

A treatment planning system computes a three dimensional array of absorbed dose value. Since there are several sources of uncertainty in dose computation, a standard relative uncertainty \( u \) is associated with treatment planning results. Thus, point doses at the center of every voxel are spread with some probability distribution over a range of values around the computed value. According to reasons pointed out in [1, 2], a rectangular probability distribution is assumed in this work.

Given a region of interest (ROI), \( u \) can be considered constant, and thus, dose expected volume histogram, define as the volume of the ROI expected to receive doses greater or equal to \( x \) equals:
Proceedings of the Second Conference on Medical Physics and Biomedical Engineering

Dose expected volume histograms are central measures of the volume encompassed by each isodoses, but other similar functions giving lateral measures can also be defined [3].

Alpha-dose volume histogram, \( \alpha-DVH \), for the region of interest \( R \), dose level \( x \), and confidence value \( \alpha \) is defined as the volume contained in \( R \) receiving a dose equal to or greater than \( x \) with a probability equal to or greater than \( 1-\alpha \). A pair of histograms such as \( \alpha-DVH \) and \( (1-\alpha)-DVH \) define a band of high probability for the volume. The formula for \( \alpha-DVH \) is:

\[
DVH^\alpha(x) = DVH\left(\frac{x}{1 + \sqrt{3}u(2\alpha - 1)}\right)
\]  

(2)

Fig. 2 shows the first of two designs of an optimization routine with uncertainty evaluation. DevH are evaluated at each iteration and checked with constraints. Each computation step is thus delayed with DevH calculation.

A different approach is to use equations (3) and (4) in order to find \( DVH \) modified constraints that would insure fulfillment of DevH and \( \alpha-DVH \) constraints, depending on the case. This way the optimization routine can take approximately the same time (because no iterative computation of DevH is needed) and additional steps are added at the beginning, when constraints are modified, and at the end, when DevH and \( \alpha-DVH \) are finally computed (Fig. 3).
uncertainty is probably a minor contribution in the overall balance (compared to organ motion or setup errors), but as Li et al have shown (6), remarkable figures of uncertainty could result when high accuracy is sought for.

The techniques presented in this work allow to manage uncertainty in the planning and evaluation process. This is the point when a choice is made and a good knowledge of uncertainty issues allows a better judgment.

5. REFERENCES


Acute Mucosal Reactions in Patients with Advanced Head and Neck Cancer Treated with Concurrent Chemoradiotherapy

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Abstract—We conducted a clinical study to analyze the acute reactions in the oral cavity and the oropharyngeal (OCOPH) mucosa in patients with advanced head and neck cancer (HNC) undergoing a definitive treatment consisted of 3-D conformal radiotherapy combined with concomitant chemotherapy. Twenty-nine patients with HNC who were treated between February 2008 and October 2009 were included in the study. The median age was 55 years (range 29-70). The site distribution was as follows: oropharynx, 20.7%; hypopharynx, 41.4%; larynx, 37.9%. The radiation technique used for 3-D conformal radiotherapy was named “oblique photon fields” technique. The OCOPH mucosa as a critical normal tissue was delineated in every patient. Extraction of planning target volume (PTV50) from the volume of OCOPH mucosa led to formation of an OCOPH mucosa with extracted PTV50 (OCOPHEx mucosa). Acute mucosal reactions were recorded using Radiation Therapy Oncology Group (RTOG) grading system. The duration of a maximum grade of reaction was also recorded. A time intensity parameter, so-called Severity-Time Units (STU), quantifying the area under the acute reaction curve, was used to express the intensity of mucositis over time in every patient.

Grade 3 acute mucosal reaction was manifested in 19 patients (65.5%). The median duration of confluent mucositis was 21 days (range 14-35). The STU less than 1000 mm² and the STU more than 1500 mm² was calculated in equal number of patients (9 patients, or 31.0%). Statistically significant difference in the distribution of the grade 3 reaction was found among patients with different site of the primary tumor (p = 0.003). Statistically significant difference was found between the grade of the acute mucositis and the volume of OCOPHEx mucosa, the dose in 50% of the volume of OCOPHEx mucosa, and the mean dose to OCOPHEx mucosa (p = 0.02, p = 0.0002, p = 0.00001, respectively). The tested relation between STU and delineated volumes (PTV50 and OCOPHEx mucosa) showed the presence of statistically significant difference (p = 0.044 and p = 0.02, respectively). Statistically significant difference was also found between STU and the mean dose to OCOPHEx mucosa (p = 0.0003). Linear regression showed negative correlation between STU and the volume of OCOPHEx mucosa (r = -0.7; p < 0.05).

The incidence and the duration of confluent mucositis were significantly greater in patients with oropharyngeal primary lesions. The intensity in time of acute mucosal reactions was significantly higher in patients with the greatest PTV50 and in those with the smallest volumes of OCOPHEx mucosa.

Keywords—acute mucositis, head and neck cancer, radiotherapy, chemotherapy

1. INTRODUCTION

Head and neck cancers (HNCs) are frequent tumors with an estimated annual global incidence of more than 550,000 cases diagnosed worldwide [1, 2]. About two-thirds of the patients are diagnosed with locoregionally advanced disease. Although radiotherapy and surgery remain the two main treatment options, the systemic therapy has become an integral part of multimodality treatment with radiotherapy and concurrent platinum-based chemoradiotherapy being an evidence-based recommended standard of care in patients with locally advanced HNC [3-5]. The intensification of radiotherapy treatment for advanced HNC using concurrent chemotherapy, has resulted in significantly improved locoregional control and survival [4-6] but these improvements are obtained at the price of increased acute toxicity due to the interaction between chemotherapy and radiotherapy [7, 8]. The increased patient morbidity, notably an increase in severe mucositis.
that cause a substantial pain and interfere with the patient’s ability to chew and swallow, inevitably worsens the patient’s quality of life [9].

Mucositis is understood as a complex interaction of mucosal injury, inflammatory response, ulceration, and healing. Acute mucositis is the result of hypoplasia of the squamous epithelium due to sterilization of mucosal stem cells and inhibition of proliferation of transit cells. In agreement with the normal cell turnover rate, the lack of supply of new cells caused by radiation, leads to a gradual, linear decrease in epithelial cell numbers [10]. If the cellularity of the mucosa drops below a certain critical level (about 70%), the cell production rate from surviving cells increases dramatically [11]. As fractionated radiotherapy continues, the cell production can not keep up with the cell killing and partial or complete denudation develops presenting as spotted or confluent mucositis. Once a peak of a confluent mucositis is reached, further increase in dose and cell killing will not produce any increase in the intensity of acute reaction, but directly influences the duration of the confluent mucositis and its healing [10, 11].

The severity and the duration of the mucositis are variable, depending on field size and shape, total dose, dose per fraction, and duration of radiotherapy. According to Van der Schueren [12], the irradiated mucosal surface, the sites treated and the general condition of the patient represent important factors influencing the mucosal reaction pattern. Also, the incidence of confluent mucositis doubles with the usage of concurrent chemoradiotherapy compared with radiotherapy alone [13].

The introduction of the conformal radiotherapy with 3-D treatment planning on computed tomography (CT) scans as the standard of practice in clinics around the world with tight target definitions of the primary tumor and neck nodal levels enables improvement of tumor coverage while sparing the surrounding critical tissues [14-16].

The aim of our study was to analyze the frequency and the intensity of the acute mucosal reactions in patients with advanced HNC treated with external-beam radiotherapy performed using a 3D conformal technique and a chemotherapy consisting of cisplatin given on a weekly basis administered concurrently with the radiotherapy course.

2. MATERIALS AND METHODS

Patient population and characteristics

A total of 29 patients with previously untreated stage III-IV HNC who received concurrent chemoradiotherapy as their primary treatment between February 2008 and October 2009 at the University Clinic of Radiotherapy and Oncology in Skopje were included in this study. Detailed patients’ characteristics are given in Table 1. The site distribution was as follows: oropharynx, 6 patients (20.7%); hypopharynx, 12 patients (41.4%); and larynx, 11 patients (37.9%). Patients were staged according to the 2002 criteria of the American Joint Committee on Cancer [17]. All patients had at least 6 months follow-up.

Table 1. Patients characteristics (n = 29)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>25 (86.2)</td>
</tr>
<tr>
<td>Female</td>
<td>4 (13.8)</td>
</tr>
<tr>
<td>Age, years</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>55</td>
</tr>
<tr>
<td>Range</td>
<td>29-70</td>
</tr>
<tr>
<td>Performance status (ECOG)</td>
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</tr>
<tr>
<td>0</td>
<td>19 (65.5)</td>
</tr>
<tr>
<td>1</td>
<td>10 (34.5)</td>
</tr>
<tr>
<td>Tracheostomy</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>10 (34.5)</td>
</tr>
<tr>
<td>No</td>
<td>19 (65.5)</td>
</tr>
<tr>
<td>Site of primary tumor</td>
<td></td>
</tr>
<tr>
<td>Oropharynx</td>
<td>6 (20.7)</td>
</tr>
<tr>
<td>Hypopharynx</td>
<td>12 (41.4)</td>
</tr>
<tr>
<td>Larynx</td>
<td>11 (37.9)</td>
</tr>
<tr>
<td>T stage</td>
<td></td>
</tr>
<tr>
<td>T3</td>
<td>11 (37.9)</td>
</tr>
<tr>
<td>T4</td>
<td>18 (62.1)</td>
</tr>
<tr>
<td>N stage</td>
<td></td>
</tr>
<tr>
<td>N0</td>
<td>13 (44.8)</td>
</tr>
<tr>
<td>N1</td>
<td>1 (3.4)</td>
</tr>
<tr>
<td>N2</td>
<td>11 (37.9)</td>
</tr>
<tr>
<td>N3</td>
<td>4 (13.8)</td>
</tr>
<tr>
<td>N− vs. N+</td>
<td></td>
</tr>
<tr>
<td>N−</td>
<td>13 (44.8)</td>
</tr>
<tr>
<td>N+</td>
<td>16 (55.2)</td>
</tr>
<tr>
<td>Stage</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>4 (13.8)</td>
</tr>
<tr>
<td>IV</td>
<td>25 (86.2)</td>
</tr>
</tbody>
</table>

ECOG, Eastern Cooperative Oncology Group.

*Because of rounding not all percentage total 100.

Treatment

Patients were immobilized in supine position with a thermoplastic head and neck mask. They were treated by photons with beam qualities of 6 MV and 15 MV and electrons with energies 9-16 MeV. For the treatment planning, we used the Eclipse Version 7.3.10, a commercial 3-D treatment planning system manufactured by Varian Medical Systems. The CT scanning was made for each patient in the treatment position with slice thickness of 0.5 cm.

The gross tumor volume of the primary tumor (GTVt70) and the metastatic lymph nodes (GTVn70) were defined as any visible tumor and the gross nodal disease revealed on imaging studies and/or physical examination. The neck lymph nodes were considered metastatic when their smallest axis diameter was greater than 1.0 cm. The clinical target volume (CTVt50) encompassed the GTVt70 plus a margin of...
Characteristics of delineated volumes

The median volume of the GTV was 91 cm$^3$ (range 29-354). The GTV ≤ 65 cm$^3$ and the GTV between 66 cm$^3$ and 130 cm$^3$ were present in equal number of patients (10, or 34.5%). The GTV more than 130 cm$^3$ was present in 9 patients (31.0%). The median value of the PTV50 was 642 cm$^3$ (range 340-936). The PTV50 more than 660 cm$^3$ was measured in almost half of the patients (12, or 41.4%). Eight patients (27.6%) had a volume of the OCOPHEx mucosa between 101 cm$^3$ and 103 cm$^3$, and 9 patients (31.0%) was with volume of the OCOPHEx mucosa more than 130 cm$^3$. Values of the volumes of the OCOPHEx mucosa according to the site of the primary tumor are summarized in Table 2. The lowest median value was seen in patients with oropharyngeal carcinoma, while the highest median value was present in patients with carcinoma of the larynx (47 cm$^3$ and 135 cm$^3$, respectively).

Table 2. Volumes of oral cavity and oropharyngeal mucosa with extracted PTV50 according to the site of the primary tumor

<table>
<thead>
<tr>
<th>Site of the primary tumor</th>
<th>No of pts</th>
<th>Volume of OCOPH mucosa with extracted PTV50 (cm$^3$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oropharynx</td>
<td>6</td>
<td>47</td>
</tr>
<tr>
<td>Hypopharynx</td>
<td>12</td>
<td>106.5</td>
</tr>
<tr>
<td>Larynx</td>
<td>11</td>
<td>135</td>
</tr>
</tbody>
</table>

Doses to oral cavity and oropharyngeal mucosa with extracted PTV50

The median values of the calculated doses were as follows: maximum dose, 71 Gy (range 54-74); mean dose, 42 Gy (range 26-64); and D50%, OCOPHEx mucosa, 47 Gy (range 22-69). Mean dose ≤ 40 Gy was delivered in 13 patients (44.8%). In the rest 16 patients (55.2%) the mean dose to the OCOPHEx mucosa was more than 40 Gy.

Assessment of acute mucositis

Weekly assessments of acute mucositis during chemoradiotherapy were performed by the radiation oncologist according to the Acute Radiation Morbidity Scoring Criteria of the Radiation Therapy Oncology Group (RTOG) (quantal descriptive scoring system from 0 to 4) [19]. Patients were also evaluated for acute mucositis during early post-irradiation follow-up visits. The severity (grade) of acute mucositis, the time to development of acute reaction (spotted or confluent mucositis i.e. days to Grade > 1), and the duration of the maximum grade of reaction were recorded. The intensity of mucositis over time was used as an additional endpoint of the normal tissue acute reaction. This time intensity parameter, so-called Severity-Time Units (STU), quantified the area under the acute reaction curve expressing grade of acute mucositis vs. time, starting at the first day of treatment up to 12 weeks following radiotherapy commencement. STU was considered to be a more appropriate indicator of the radiosensitivity
of a normal mucosa incorporating the severity of acute mucosal reaction and its kinetics i.e. the time to maximum grade of acute mucositis, its duration, and the time of healing. For each patient, grades of mucositis were plotted as a function of time at day 1 through day 84. Adjacent data points were then connected using straight line segments, and the STU as an area under the curve was calculated. So, mathematically, the STU was the sum of consecutive severity-scores multiplied by their duration in days.

Statistical analysis

In the analysis of the significant differences between the grade of acute mucosal reaction and tumor characteristics, delineated target volumes, volume of OCOPHEx mucosa, and doses delivered to OCOPHEx mucosa, Chi-square test or Fisher exact test were used. Significant differences between the duration of confluent mucositis and tumor characteristics and delineated target volumes were tested with Mann-Whitney U test or Fisher exact test. Significant differences between the STU and characteristics of delineated target volumes, volume of OCOPHEx mucosa, and the doses delivered to OCOPHEx mucosa were tested with Kruskal-Wallis ANOVA or Chi-square test. Correlation between STU and the volume of OCOPHEx mucosa and between STU and the mean dose delivered to the volume of OCOPHEx mucosa was tested by linear regression.

3. RESULTS

Characteristics of acute reactions in OCOPH mucosa are summarized in Table 3. Confluent mucositis (grade 3 reaction) as a maximum grade of reaction was manifested in 19 patients (65.5%). The median time to development of confluent mucositis was 21 days (range 14-21). The median duration of confluent mucositis was 21 days (range 14-35). In almost two thirds of patients (12, or 63.2%) the duration of the grade 3 reaction was \( \leq \) 21 days. The STU less than 1000 mm\(^2\) and the STU more than 1500 mm\(^2\) were calculated in equal number of patients (9, or 31.0%).

There was a statistically significant difference found in the distribution of the acute mucosal reactions among patients with different sites of the primary tumor (Chi-square test; \( p = 0.003 \)) (Table 4). The confluent mucositis was significantly more expressed in patients with oropharyngeal and hypopharyngeal primary lesions. The grade of the acute mucosal reactions significantly differed among the three classes of the volume of OCOPHEx mucosa (Chi-square test; \( p = 0.02 \)) (Table 4). The incidence of confluent mucositis was significantly higher in patients with volume of OCOPHEx mucosa \( \leq \) 100 cm\(^3\). A significant difference existed between the grade of the acute mucositis and the D50%, OCOPHEx mucosa, and between the grade of the mucositis and the mean dose to the volume of OCOPHEx mucosa (Fisher exact test; \( p = 0.0002 \) and \( p = 0.0001 \), respectively) (Table 4). The confluent mucositis was significantly more expressed in patients with D50%, OCOPHEx mucosa > 45 Gy and in those with a mean dose in OCOPHEx mucosa being > 40 Gy.

Table 3. Characteristics of acute reactions in oral cavity and oropharyngeal mucosa

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum grade of reaction (n = 29)</td>
<td></td>
</tr>
<tr>
<td>Grade 2</td>
<td>10 (34.5)</td>
</tr>
<tr>
<td>Grade 3</td>
<td>19 (65.5)</td>
</tr>
<tr>
<td>Time to grade 2 reaction, days</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>21</td>
</tr>
<tr>
<td>Range</td>
<td>14-28</td>
</tr>
<tr>
<td>Duration of grade 2 reaction, days</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>14</td>
</tr>
<tr>
<td>Range</td>
<td>14-28</td>
</tr>
<tr>
<td>Time to grade 3 reaction, days</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>21</td>
</tr>
<tr>
<td>Range</td>
<td>14-21</td>
</tr>
<tr>
<td>Time to grade 3 reaction (n = 19)</td>
<td></td>
</tr>
<tr>
<td>( \leq ) 14 days</td>
<td>5 (26.3)</td>
</tr>
<tr>
<td>( &gt; ) 14 days</td>
<td>14 (73.7)</td>
</tr>
<tr>
<td>Duration of grade 3 reaction, days</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>21</td>
</tr>
<tr>
<td>Range</td>
<td>14-35</td>
</tr>
<tr>
<td>Duration of grade 3 reaction (n = 19)</td>
<td></td>
</tr>
<tr>
<td>( \leq ) 21 days</td>
<td>12 (63.2)</td>
</tr>
<tr>
<td>( &gt; ) 21 days</td>
<td>7 (36.8)</td>
</tr>
<tr>
<td>Severity-Time Units (STU) (n = 29)</td>
<td></td>
</tr>
<tr>
<td>( &lt; ) 1000 mm(^3)</td>
<td>9 (31.0)</td>
</tr>
<tr>
<td>1000-1500 mm(^3)</td>
<td>11 (38.0)</td>
</tr>
<tr>
<td>( &gt; ) 1500 mm(^3)</td>
<td>9 (31.0)</td>
</tr>
</tbody>
</table>

A statistically significant difference was found between the duration of the grade 3 acute mucositis and the site of the primary tumor and between the duration of the grade 3 acute mucositis and the PTV70 (Mann-Whitney U test; \( p = 0.013 \) and \( p = 0.047 \), respectively) (Table 5). The duration of grade 3 mucositis > 21 days was apparently more represented in patients with oropharyngeal cancer and in those with PTV70 > 200 cm\(^2\).

When testing the differences between STU and delineated volumes we found the existence of a statistically significant difference between STU and PTV50 and between STU and the volume of OCOPHEx mucosa (Kruskal-Wallis ANOVA; \( p = 0.044 \) and \( p = 0.02 \), respectively), showing that intensity in time of acute mucosal reactions was significantly higher in patients with the greatest PTV50 and in those cases with the smallest volumes of OCOPHEx mucosa (Table 6).
The presence of a negative correlation between STU and the volume of OCOPHEx mucosa was confirmed with linear regression \( r = -0.7; p < 0.05 \) (Fig. 1).

There was also a statistically significant difference found between STU and the D50%, OCOPHEx mucosa and between STU and the mean dose to the volume of OCOPHEx mucosa (Chi-square test; \( p = 0.0001 \) and \( p = 0.0003 \), respectively) (Table 6). Correlation between STU and the mean dose delivered to the volume of OCOPHEx mucosa was confirmed with linear regression \( r = 0.9; p < 0.05 \) (Fig. 2).

### Table 4. Grades of maximal acute mucosal reaction according to tumor and treatment characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Grade of mucosal reaction</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site of the primary tumor</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oropharynx</td>
<td>6</td>
<td>0 (0.0)</td>
<td>6 (100.0)</td>
<td></td>
</tr>
<tr>
<td>Hypopharynx</td>
<td>12</td>
<td>2 (16.7)</td>
<td>10 (83.3)</td>
<td>0.003</td>
</tr>
<tr>
<td>Larynx</td>
<td>11</td>
<td>8 (72.7)</td>
<td>3 (27.3)</td>
<td></td>
</tr>
<tr>
<td>T stage</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T3</td>
<td>11</td>
<td>4 (36.4)</td>
<td>7 (63.6)</td>
<td>0.590</td>
</tr>
<tr>
<td>T4</td>
<td>18</td>
<td>6 (33.3)</td>
<td>12 (66.7)</td>
<td></td>
</tr>
<tr>
<td>N- vs N+</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N-</td>
<td>13</td>
<td>7 (53.8)</td>
<td>6 (46.2)</td>
<td>0.064</td>
</tr>
<tr>
<td>N+</td>
<td>16</td>
<td>3 (18.8)</td>
<td>13 (81.2)</td>
<td></td>
</tr>
<tr>
<td>Stage</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>4</td>
<td>3 (75.0)</td>
<td>1 (25.0)</td>
<td>0.100</td>
</tr>
<tr>
<td>IV</td>
<td>25</td>
<td>7 (28.0)</td>
<td>18 (72.0)</td>
<td></td>
</tr>
<tr>
<td>PTV50 (cm³)</td>
<td>≤ 500</td>
<td>6</td>
<td>4 (66.7)</td>
<td>2 (33.3)</td>
</tr>
<tr>
<td></td>
<td>501-660</td>
<td>12</td>
<td>4 (33.3)</td>
<td>8 (66.7)</td>
</tr>
<tr>
<td></td>
<td>&gt; 660</td>
<td>11</td>
<td>2 (18.2)</td>
<td>9 (81.8)</td>
</tr>
<tr>
<td>PTV70 (cm³)</td>
<td>≤ 130</td>
<td>8</td>
<td>4 (50.0)</td>
<td>4 (50.0)</td>
</tr>
<tr>
<td></td>
<td>131-200</td>
<td>12</td>
<td>5 (41.7)</td>
<td>7 (58.3)</td>
</tr>
<tr>
<td></td>
<td>&gt; 200</td>
<td>9</td>
<td>1 (11.1)</td>
<td>8 (88.9)</td>
</tr>
<tr>
<td>Volume of OCOPHEx mucosa with extracted PTV% (cm³)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 100</td>
<td>12</td>
<td>1 (8.3)</td>
<td>11 (91.7)</td>
<td></td>
</tr>
<tr>
<td>101-130</td>
<td>8</td>
<td>3 (37.5)</td>
<td>5 (62.5)</td>
<td>0.020</td>
</tr>
<tr>
<td>&gt; 130</td>
<td>9</td>
<td>6 (66.7)</td>
<td>3 (33.3)</td>
<td></td>
</tr>
<tr>
<td>Dose in 50% volume of OCOPHEx mucosa (Gy)</td>
<td></td>
<td></td>
<td></td>
<td>0.0002</td>
</tr>
<tr>
<td>≤ 45</td>
<td>12</td>
<td>9 (75.0)</td>
<td>3 (25.0)</td>
<td></td>
</tr>
<tr>
<td>&gt; 45</td>
<td>17</td>
<td>1 (5.9)</td>
<td>16 (94.1)</td>
<td></td>
</tr>
<tr>
<td>Mean dose to OCOPHEx mucosa (Gy)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 40</td>
<td>13</td>
<td>10 (76.9)</td>
<td>3 (23.1)</td>
<td>0.00001</td>
</tr>
<tr>
<td>&gt; 40</td>
<td>16</td>
<td>0 (0.0)</td>
<td>16 (100.0)</td>
<td></td>
</tr>
</tbody>
</table>

PTV, planning target volume; OCOPHEx mucosa, oral cavity and oropharyngeal mucosa with extracted PTV50.

### Table 5. Duration of grade 3 reaction according to tumor and treatment characteristics (n = 19)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Duration of grade 3 mucositis (days)</th>
<th>≤ 21</th>
<th>&gt; 21</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site of the primary tumor</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oropharynx</td>
<td>6</td>
<td>1 (16.7)</td>
<td>5 (83.3)</td>
<td>0.013</td>
</tr>
<tr>
<td>Hypopharynx</td>
<td>10</td>
<td>8 (80.0)</td>
<td>2 (20.0)</td>
<td></td>
</tr>
<tr>
<td>Larynx</td>
<td>3</td>
<td>3 (100.0)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>T stage</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T3</td>
<td>7</td>
<td>4 (57.1)</td>
<td>3 (42.9)</td>
<td>0.110</td>
</tr>
<tr>
<td>T4</td>
<td>12</td>
<td>8 (66.7)</td>
<td>4 (33.3)</td>
<td></td>
</tr>
<tr>
<td>N- vs N+</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N-</td>
<td>6</td>
<td>5 (83.3)</td>
<td>1 (16.7)</td>
<td>0.332</td>
</tr>
<tr>
<td>N+</td>
<td>13</td>
<td>7 (53.8)</td>
<td>6 (46.2)</td>
<td></td>
</tr>
<tr>
<td>Stage</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>1</td>
<td>1 (100.0)</td>
<td>0 (0.0)</td>
<td>0.631</td>
</tr>
<tr>
<td>IV</td>
<td>18</td>
<td>11 (61.1)</td>
<td>7 (38.9)</td>
<td></td>
</tr>
<tr>
<td>PTV50 (cm³)</td>
<td>≤ 500</td>
<td>2</td>
<td>2 (100.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td></td>
<td>501-660</td>
<td>8</td>
<td>6 (75.0)</td>
<td>2 (25.0)</td>
</tr>
<tr>
<td></td>
<td>&gt; 660</td>
<td>9</td>
<td>4 (44.4)</td>
<td>5 (55.6)</td>
</tr>
<tr>
<td>PTV70 (cm³)</td>
<td>≤ 130</td>
<td>4</td>
<td>4 (100.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td></td>
<td>131-200</td>
<td>7</td>
<td>5 (71.4)</td>
<td>2 (28.6)</td>
</tr>
<tr>
<td></td>
<td>&gt; 200</td>
<td>8</td>
<td>3 (37.5)</td>
<td>5 (62.5)</td>
</tr>
</tbody>
</table>

PTV, planning target volume.

Correlation: \( r = -0.6614 \)

Correlation: \( r = 0.89783 \)
Table 6. Severity-Time Units according to treatment characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total number of patients</th>
<th>Number of patients (%)</th>
<th>STU (mm²)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>&lt; 1000</td>
<td>1000-1500</td>
</tr>
<tr>
<td>PTV50 ≤ 500</td>
<td>6</td>
<td>4 (66.7)</td>
<td>2 (33.3)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td></td>
<td>501-660</td>
<td>2 (18.2)</td>
<td>3 (27.3)</td>
<td>6 (54.5)</td>
</tr>
<tr>
<td></td>
<td>&gt; 660</td>
<td>1 (11.1)</td>
<td>3 (33.3)</td>
<td>5 (55.6)</td>
</tr>
<tr>
<td>PTV70 ≤ 130</td>
<td>8</td>
<td>3 (37.5)</td>
<td>4 (50.0)</td>
<td>1 (12.5)</td>
</tr>
<tr>
<td></td>
<td>131-200</td>
<td>5 (41.7)</td>
<td>4 (33.3)</td>
<td>3 (25.0)</td>
</tr>
<tr>
<td></td>
<td>&gt; 200</td>
<td>1 (11.1)</td>
<td>1 (11.1)</td>
<td>3 (33.3)</td>
</tr>
<tr>
<td>Volume of OCOPHEx mucosa (cm³) ≤ 100</td>
<td>12</td>
<td>1 (8.3)</td>
<td>4 (33.3)</td>
<td>7 (58.3)</td>
</tr>
<tr>
<td></td>
<td>101-130</td>
<td>3 (37.5)</td>
<td>4 (50.0)</td>
<td>1 (12.5)</td>
</tr>
<tr>
<td></td>
<td>&gt; 130</td>
<td>5 (55.6)</td>
<td>3 (33.3)</td>
<td>1 (11.1)</td>
</tr>
<tr>
<td>Dose in 50% volume of OCOPHEx mucosa (Gy) ≤ 45</td>
<td>12</td>
<td>9 (75.0)</td>
<td>2 (16.7)</td>
<td>1 (8.3)</td>
</tr>
<tr>
<td></td>
<td>&gt; 45</td>
<td>0 (0.0)</td>
<td>9 (52.9)</td>
<td>8 (47.1)</td>
</tr>
<tr>
<td>Mean dose to OCOPHEx mucosa (Gy) ≤ 40</td>
<td>16</td>
<td>9 (69.2)</td>
<td>3 (23.1)</td>
<td>1 (7.7)</td>
</tr>
<tr>
<td></td>
<td>&gt; 40</td>
<td>0 (0.0)</td>
<td>8 (50.0)</td>
<td>8 (50.0)</td>
</tr>
</tbody>
</table>

PTV, planning target volume; STU, Severity-Time Units; OCOPHEx mucosa, oral and oropharyngeal mucosa with extracted PTV50.
*Because of rounding not all percentage total 100.

4. CONCLUSION

Considering the results of our study we take the liberty to recommend delineation of OCOPH mucosa to be established as a routine procedure in contouring normal tissue volumes. This procedure, in conditions of implemented Intensity Modulated Radiation Therapy (IMRT), is expected to enable delivering doses equal or less that 40 Gy at OCOPHEx mucosa in order to prevent a high incidence of confluent mucositis. Regarding the results that showed the incidence of the confluent mucositis and it’s intensity in time being significantly higher in patients with smallest volumes of OCOPHEx mucosa and taking into account that the incidence and the duration of the confluent mucositis were significantly greater in patients with oropharyngeal primary lesions, we can conclude that this procedure would be expected to be most valuable in this patients’ category that is characterized with the lowest median value of OCOPHEx mucosa.

5. REFERENCES

[9] Trotti A et al., Mucositis incidence, severity and associated outcomes in patients with head and neck cancer receiving radiotherapy with or...


A TREATMENT PLANNING COMPARISON OF TWO DIFFERENT 3D CONFORMAL TECHNIQUES FOR IRRADIATION OF HEAD AND NECK CANCER PATIENTS

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¹ University Clinic for Radiotherapy and Oncology, Vodnjanska 17, Skopje, R. Macedonia, duskol@yahoo.com, krstevskav@gmail.com, pet.sonja@gmail.com

Abstract – The purpose of this treatment planning study was to compare two different three dimensional conformal irradiation techniques for head and neck cancer patients. For 33 patients with head and neck carcinoma, irradiated according to the classical technique, we computed and evaluated a second irradiation technique in order to optimize the treatment planning protocol. The classical technique, termed “electron-photon fields”, employed two lateral semi-fields (23 fractions) for irradiation of the upper part of the planning target volume that should receive 50 Gy (PTV50) and an anterior and posterior field for the lower part. After the 23rd fraction the lateral fields were reduced from the dorsal side (2 fractions), in order to exclude the spinal cord from them. At the same time the dose to the shielded part of the target volume was delivered with matched electron fields. Finally, after the 25th fraction, the high risk volume was irradiated to the desired dose with plan where the spinal cord was completely shielded. In the new technique, termed “oblique photon fields”, 4 oblique isocentric photon fields were used (25 fractions): two anterior fields that covered the entire target volume that should receive 50 Gy and two posterior fields that covered only half of the target volume in order to shield the spinal cord. Thus, the necessity for using electron fields is eliminated. We kept the plan for irradiation of the high risk planning target volume the same as in the classical technique. The prescribed dose per fraction in all plans was 2 Gy. In both techniques the plans were optimized to the same maximal point dose and the same dose to the spinal cord.

The oblique fields plan showed better coverage and homogeneity of the PTV50, except for the patients with positive resection margins receiving postoperative radiotherapy (receiving 66 Gy), where the coverage did not differ significantly. The conformity in both techniques did not differ significantly. The mean dose to the parotid glands was significantly smaller with the oblique fields plan in case of patients with negative resection margins and when all the patients were treated as one group.

The preferred treatment technique is thus the oblique photon fields technique, not only because of the superior dosimetric parameters, but also because of the absence of the electron fields which complicate the entire treatment process from dosimetric as well as practical aspect.

Keywords – treatment planning, head and neck cancer, 3D conformal radiotherapy

1. INTRODUCTION

The radiation treatment of the patients with head and neck cancer is considered one of the most challenging treatments in radiotherapy. One of the reasons for that is the anatomy of the body itself, where the volume that should be irradiated is located, ranging from the thick bony structures at the face, through the thin rounded contour of the upper neck, to the thick flatter surface of the supraclavicular areas. The other reason, which is the main reason, is that the volume that should be irradiated has a convex shape encompassing the spinal cord, which is the most critical organ at risk (OAR) at this site. The maximal dose tolerated by the spinal cord is considered to be between 45 Gy and 50 Gy. The presence of the other OAR like the oral cavity and the parotid glands, complicate the treatment further.

The classical approach in the treatment of this complex convex shape of the planning target volume (PTV) is to irradiate it up to the maximal allowable dose with two lateral photon fields (usually of 6 MV) and then to reduce the fields from the dorsal side in order to spare the spinal cord. The part of the PTV that remains outside of the reduced fields is then irradiated by electron fields of suitable energy (usually 9 MeV) that are matched to the photon fields. Such a protocol was adopted at our institution as well.
However such an approach has certain downsides. The first downside is of dosimetric nature. When an electron field is matched to a photon field a hot spot develops on the side of the photon field because of the outscattering of electrons from the electron field. This hotspot can be up to 125% of the prescribed dose. The second downside is of technical nature. Namely, for the electron fields one must mould the customized blocks that correspond precisely to the planned field. In practice, the accuracy of the molding can not be better than 1-2 mm. This can lead to additional hot or cold spots during the treatment. And finally, there is a practical aspect of increasing the workload of the department.

To overcome these difficulties we conducted a treatment planning study where we compared this classical approach to a new technique using 4 oblique photon fields, eliminating the need for electron fields [1-4] and their matching to the corresponding photon fields. In the comparison of the two protocols we name the classical approach as “electron – photon” technique (EPT) and the new one, which is under investigation, as “oblique photon fields” technique (OPFT).

2. MATERIALS AND METHODS

2.1. Patient population and contouring

A total of 33 patients were included in this study. The patient characteristics are given in Table 1 and the type of radiotherapy in Table 2.

Table 1. Patient characteristics (n=33)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>32 (97)</td>
</tr>
<tr>
<td>Female</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Site of primary tumor</td>
<td></td>
</tr>
<tr>
<td>Cavum oris</td>
<td>6 (18.2)</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>3 (9.1)</td>
</tr>
<tr>
<td>Hypopharynx</td>
<td>8 (24.2)</td>
</tr>
<tr>
<td>Larynx</td>
<td>16 (48.5)</td>
</tr>
<tr>
<td>T stage</td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>3 (9.1)</td>
</tr>
<tr>
<td>T3</td>
<td>12 (36.4)</td>
</tr>
<tr>
<td>T4</td>
<td>18 (54.5)</td>
</tr>
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<td>N stage</td>
<td></td>
</tr>
<tr>
<td>N- vs. N+</td>
<td></td>
</tr>
<tr>
<td>N−</td>
<td>25 (75.8)</td>
</tr>
<tr>
<td>N+</td>
<td>8 (24.2)</td>
</tr>
<tr>
<td>Stage</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>1 (3)</td>
</tr>
<tr>
<td>III</td>
<td>11 (33.3)</td>
</tr>
<tr>
<td>IV</td>
<td>21 (63.6)</td>
</tr>
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</table>

Table 2. Type of radiotherapy

<table>
<thead>
<tr>
<th>Type of radiotherapy</th>
<th>Number of patients (%)</th>
<th>Prescribed dose (Gy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postoperative radiotherapy if negative resection margins and negative neck</td>
<td>10 (30.3)</td>
<td>60</td>
</tr>
<tr>
<td>Postoperative radiotherapy if close or positive resection margins and metastatic lymph nodes in the neck</td>
<td>10 (30.3)</td>
<td>66</td>
</tr>
<tr>
<td>Definitive radiotherapy</td>
<td>13 (39.4)</td>
<td>70</td>
</tr>
</tbody>
</table>

In patients who were planned for postoperative radiotherapy and there were no positive resection margins and nodal involvement (PRNR), the clinical target volume (CTV_{60}) encompassed the bed of the primary tumor. In patients who were planned for postoperative radiotherapy but there were close or positive margins of resection of the primary tumor as well as metastatic lymph nodes in the neck (PRPR), CTV_{60} represented an union of CTV_{66} that encompassed the bed of the primary tumor and CTV_{66} that encompassed the area of neck dissection. In patients who were candidates for definitive radiotherapy (DR), the gross tumor volume of the primary tumor (GTVt_{70}) and the metastatic lymph nodes (GTVn_{70}) were defined as any visible tumor and the gross nodal disease revealed on imaging studies and/or physical examination. CTV_{50} encompassed the GTVt_{70} plus a margin of 1.0-2.0 cm for the potential microscopic extension of the disease. In all the patients with negative neck lymph nodes irrespectively of the type of planned radiotherapy, CTVn_{50} included the nodal regions in the neck at I-III/IV for oral cavity cancers, II-IV for oropharyngeal and laryngeal cancers and I-IV for hypopharyngeal cancers [5, 6]. In surgically treated patients with positive lymph nodes, CTVn_{60} included CTVn_{50} and encompassed retropharyngeal lymph nodes and nodal regions at levels I-V. In patients with clinically involved neck lymph nodes who were not treated surgically, CTVn_{50} included GTVn_{70} with a margin of 0.5-1.0 cm and also encompassed retropharyngeal lymph nodes and nodal regions at levels I-V. Level VI was included in CTVn_{50} in all the cases when primary tumor invaded subgllotis or esophagus. The planning target volumes were PTV_{50}, PTV_{60}, PTV_{66} and PTV_{70}. The PTV_{50}, PTV_{60}, and PTV_{66} provided a margin of 0.5 cm around CTV_{50}, CTV_{60} and CTV_{66}, respectively. In patients planned for definitive radiotherapy, when there were no positive lymph nodes in the neck, the PTV_{70} encompassed the GTVt_{70} plus a 0.5 cm margin. In patients with nodal disease, the GTV_{70} was union of GTVt_{70} and GTVn_{70} and by adding a margin of 0.5 cm around it, we obtained PTV_{70}. The parotid glands, as organs at risk, were delineated separately. The spinal cord was delineated with
diameter of 1.4 cm and a margin of 0.3 cm was added to create Planning Organ at Risk Volume (PRV_spinal).

2.2. Description of the treatment techniques

Each of the 30 patients included in this treatment planning study was irradiated according to the EPT technique, which was the standing protocol at our institution. For each of them a second plan was computed and evaluated according to the OPFT technique. The treatment planning was conducted using the Eclipse Version 7.3.10, a commercial 3-D treatment planning system manufactured by Varian Medical Systems. In both techniques, the planned dose per fraction in all the treatment plans was 2 Gy.

2.2.1. Electron – photon technique

The EPT consists of three stages. In the first stage (23 fractions), we used 4 photon semi fields: two opposing lateral semi-fields of equal weights with beam qualities of 6 MV for the upper neck, and anterior and posterior semi-fields for the lower neck. For the anterior field we used 6 MV photons and for the posterior 15 MV photons, with Varian Medical Systems. In both techniques, the planned dose per fraction in all the treatment plans was 2 Gy.

2.2.2. Oblique photon fields technique

The OPFT consists of two stages. In the first stage (25 fractions), we used 4 oblique isocentric photon fields of beam qualities 6 MV. Two of the fields, the anterior ones, were positioned at gantry angles 300° and 60° and covered the whole PTV50. The posterior oblique fields were at gantry angles between 210° and 220° from the right side of the patient, and between 135° and 145° from the left side. The spinal cord was shielded in these fields, so they covered only part of the PTV50. The weight of the posterior fields was reduced from the dorsal side in order to exclude the spinal cord from the fields. The dose to the shielded dorsal part of the PTV50 was delivered by two lateral electron fields, which were matched to the photon fields. Depending on the patient anatomy, the electron fields were of energies 9 MeV and rarely 12 MeV. In the third stage of the treatment plan (5, 8 or 10 fractions), depending on the position and the volume of the PTV60, PTV66 or PTV70, we used arrangements with 2 to 4 photon fields in lateral or oblique directions with occasional use of electron fields. In this stage the spinal cord was completely out of field.

2.3. Plan evaluation and comparison

The first criterion in the optimization of the treatment plans was the maximal dose to the spinal cord. In both techniques the maximal dose to the PRV_Spinal was equal and it was less then 50 Gy. The second criterion was the global dose maximum – in both techniques the global dose maxima in the corresponding plans was equal. The dose volume histogram (DVH) analysis was applied to both PTVs and OARs for each patient. The PTVs were analyzed in terms of coverage, conformity and homogeneity. Since the treatment plan for irradiation of the high risk volume (stage three in EPT and stage two in OPFT) was the same in both techniques, the analysis was performed only on the part of the treatment plans delivering 50 Gy. The conformity and homogeneity was evaluated only for PTV50.

The analysis was performed for each of the three types of radiotherapy separately (Table 2) and also for all the patients as one sample. In the last case the PTV60, PTV66 and PTV70 are all termed as PTVboost. For evaluation of the coverage of the target volumes PTV50, PTV60, PTV66, PTV70 and PTVboost, we used the volumes receiving 47.5 Gy, 50 Gy and 52.5 Gy (i.e. 95%, 100% and 105% of the prescribed dose). The notation that we use for the volume receiving X Gy is V_X. We also compared the mean doses of the PTVs in both techniques.

For the conformity analysis we used two criteria – the conformity index (CI_RTOG) as defined by the RTOG [7] and the conformity number (CN) as introduced by van’t Riet [8, 9]. The CI_RTOG was calculated as the ratio of the volume receiving 95% of 50 Gy i.e. 47.5 Gy and the volume of the PTV50. Because the CI_RTOG fails in cases of insufficient coverage, we used the CN, which is a product of the coverage factor and the healthy tissue conformity index. The coverage factor is defined as the ratio of the volume of the part of the PTV50 receiving 47.5 Gy and the whole volume of the PTV50. The healthy tissue conformity index is defined as the ratio of the volume of PTV50 receiving 47.5 Gy and the total volume of the body receiving 47.5 Gy.

For the homogeneity analysis we also used two indices. The homogeneity index (HI) is defined as the ratio of the dose received by the 95% of the PTV50 (D95%) to the minimum dose received by the “hottest” 5% of the PTV50 (D3%). The homogeneity index HI_Wu as defined by Wu et al. [10] is used in intensity modulated radiotherapy studies for head and neck. It is defined as:

\[
HI_{Wu} = \frac{D_{95%} - D_{98%}}{D_{prescription}}
\]  

(1)

Where D95% is the minimum dose received by the “hottest” 2% of the PTV50, D98%, is the dose received by the 98% of the PTV50 and Dprescription is the prescribed dose (50 Gy).

From the OAR we compared the mean dose to the parotids.

In the analysis we compared the respective physical quantities by the non-parametric Wilcoxon exact signed rank test. Statistical significance was assumed at the level of p ≤ 0.05.
3. RESULTS AND DISCUSSION

The mean volumes of the PTVs and of the parotids are given in Table 3.

Table 3. Mean volumes and standard deviations

<table>
<thead>
<tr>
<th></th>
<th>PRNR</th>
<th>PRPR</th>
<th>DR</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTV(_{50})</td>
<td>417.5 ± 64.1</td>
<td>493.1 ± 97.3</td>
<td>600.9 ± 137.5</td>
<td>512.7 ± 130.5</td>
</tr>
<tr>
<td>PTV(_{60})</td>
<td>104.1 ± 20.0</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>PTV(_{66})</td>
<td>—</td>
<td>183.1 ± 84.7</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>PTV(_{70})</td>
<td>—</td>
<td>—</td>
<td>160.8 ± 81.0</td>
<td>—</td>
</tr>
<tr>
<td>PTV(_{boost})</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>150.4 ± 75.1</td>
</tr>
<tr>
<td>V(_\text{left parotid})</td>
<td>14.6 ± 4.3</td>
<td>12.3 ± 5.4</td>
<td>9.5 ± 4.4</td>
<td>11.9 ± 5.0</td>
</tr>
<tr>
<td>V(_\text{right parotid})</td>
<td>17.2 ± 2.6</td>
<td>13.7 ± 6.1</td>
<td>10.9 ± 3.1</td>
<td>13.6 ± 4.8</td>
</tr>
</tbody>
</table>

In Table 4 the mean values of the physical quantities defined above and the \(p\) value for the corresponding mean comparison for the patients with PRNR are given. The parameters referring to PTV\(_{50}\) were significantly greater in the OPFT, with the exception of \(V\(_{50}\)\. This means that keeping the same global maximum and the same dose to the spinal cord, we can irradiate the PTV\(_{50}\) to greater dose with this technique. Even though the mean values for PTV\(_{60}\) were greater in EPT, the differences were not significant. The only exception here was again the \(V\(_{50}\)\. There was no significant difference in the conformity, but the homogeneity was better with OPFT. The parotid glands were also spared more with OPFT.

Table 4. Dosimetric comparison of the techniques for patients with PRNR

<table>
<thead>
<tr>
<th></th>
<th>OPFT</th>
<th>EPT</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTV(_{50})</td>
<td>V(_{47.5})%</td>
<td>92.1 ± 4.8</td>
<td>89.5 ± 4.6</td>
</tr>
<tr>
<td></td>
<td>V(_{50})%</td>
<td>65.9 ± 10.7</td>
<td>63.7 ± 8.6</td>
</tr>
<tr>
<td></td>
<td>V(_{52.5})%</td>
<td>16.5 ± 4.5</td>
<td>11.5 ± 4.1</td>
</tr>
<tr>
<td></td>
<td>D(_\text{mean}) (Gy)</td>
<td>50.5 ± 0.6</td>
<td>50.2 ± 0.5</td>
</tr>
<tr>
<td>PTV(_{60})</td>
<td>V(_{47.5})%</td>
<td>96.2 ± 3.1</td>
<td>97.2 ± 2.1</td>
</tr>
<tr>
<td></td>
<td>V(_{50})%</td>
<td>84.8 ± 6.2</td>
<td>89.2 ± 6.1</td>
</tr>
<tr>
<td></td>
<td>V(_{52.5})%</td>
<td>40.1 ± 13.0</td>
<td>36.5 ± 10.0</td>
</tr>
<tr>
<td></td>
<td>D(_\text{mean}) (Gy)</td>
<td>51.7 ± 0.6</td>
<td>51.8 ± 0.4</td>
</tr>
<tr>
<td>C(_\text{RTGOG})</td>
<td>1.92 ± 0.18</td>
<td>1.81 ± 0.15</td>
<td>0.114</td>
</tr>
<tr>
<td>CN</td>
<td>0.45 ± 0.05</td>
<td>0.45 ± 0.06</td>
<td>0.767</td>
</tr>
<tr>
<td>HI</td>
<td>0.87 ± 0.03</td>
<td>0.86 ± 0.03</td>
<td>0.012</td>
</tr>
<tr>
<td>HI(_\text{Wu})</td>
<td>0.19 ± 0.04</td>
<td>0.22 ± 0.04</td>
<td>0.005</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Left</th>
<th>Right</th>
<th>Left</th>
<th>Right</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parotids</td>
<td>D(_\text{mean}) (Gy)</td>
<td>35.7 ± 6.9</td>
<td>39.3 ± 6.2</td>
<td>0.009</td>
</tr>
<tr>
<td></td>
<td>D(_\text{mean}) (Gy)</td>
<td>37.0 ± 6.0</td>
<td>39.6 ± 6.1</td>
<td>0.009</td>
</tr>
</tbody>
</table>

In Table 5 the same parameters are given, but for patients with PRPR. No significant difference in any of the dosimetric parameters could be seen, except for the homogeneity, where the OPFT shows superiority.

Table 5. Dosimetric comparison of the techniques for patients with PRPR

<table>
<thead>
<tr>
<th></th>
<th>OPFT</th>
<th>EPT</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTV(_{50})</td>
<td>V(_{47.5})%</td>
<td>88.7 ± 4.8</td>
<td>87.1 ± 1.5</td>
</tr>
<tr>
<td></td>
<td>V(_{50})%</td>
<td>58.0 ± 13.2</td>
<td>58.5 ± 7.1</td>
</tr>
<tr>
<td></td>
<td>V(_{52.5})%</td>
<td>12.5 ± 8.7</td>
<td>9.7 ± 5.8</td>
</tr>
<tr>
<td></td>
<td>D(_\text{mean}) (Gy)</td>
<td>50.1 ± 0.6</td>
<td>50.1 ± 0.6</td>
</tr>
<tr>
<td>PTV(_{66})</td>
<td>V(_{47.5})%</td>
<td>95.9 ± 3.0</td>
<td>96.3 ± 2.4</td>
</tr>
<tr>
<td></td>
<td>V(_{50})%</td>
<td>75.3 ± 15.5</td>
<td>79.6 ± 7.9</td>
</tr>
<tr>
<td></td>
<td>V(_{52.5})%</td>
<td>27.2 ± 19.5</td>
<td>20.6 ± 8.2</td>
</tr>
<tr>
<td></td>
<td>D(_\text{mean}) (Gy)</td>
<td>51.1 ± 0.8</td>
<td>51.1 ± 0.4</td>
</tr>
<tr>
<td>C(_\text{RTGOG})</td>
<td>1.81 ± 0.28</td>
<td>1.81 ± 0.26</td>
<td>0.878</td>
</tr>
<tr>
<td>CN</td>
<td>0.44 ± 0.06</td>
<td>0.43 ± 0.05</td>
<td>0.093</td>
</tr>
<tr>
<td>HI</td>
<td>0.86 ± 0.02</td>
<td>0.84 ± 0.02</td>
<td>0.030</td>
</tr>
<tr>
<td>HI(_\text{Wu})</td>
<td>0.21 ± 0.02</td>
<td>0.22 ± 0.02</td>
<td>0.028</td>
</tr>
</tbody>
</table>

Parotids

<table>
<thead>
<tr>
<th></th>
<th>Left</th>
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<th>Left</th>
<th>Right</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>D(_\text{mean}) (Gy)</td>
<td>42.2 ± 8.2</td>
<td>44.3 ± 5.9</td>
<td>0.086</td>
</tr>
<tr>
<td></td>
<td>D(_\text{mean}) (Gy)</td>
<td>40.9 ± 6.6</td>
<td>42.4 ± 5.4</td>
<td>0.214</td>
</tr>
</tbody>
</table>

The same parameters for the patients receiving DR are given in Table 6. All the parameters referring to PTV\(_{50}\) were significantly greater in the OPFT. In this patient category, by using OPFT we can also irradiate the PTV\(_{50}\) to greater dose keeping the global dose maximum and the dose to spinal cord the same.

Table 6. Dosimetric comparison of the techniques for patients receiving DR

<table>
<thead>
<tr>
<th></th>
<th>OPFT</th>
<th>EPT</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTV(_{50})</td>
<td>V(_{47.5})%</td>
<td>90.8 ± 3.5</td>
<td>86.0 ± 4.0</td>
</tr>
<tr>
<td></td>
<td>V(_{50})%</td>
<td>62.1 ± 8.5</td>
<td>53.1 ± 5.9</td>
</tr>
<tr>
<td></td>
<td>V(_{52.5})%</td>
<td>12.7 ± 5.4</td>
<td>8.6 ± 3.4</td>
</tr>
<tr>
<td></td>
<td>D(_\text{mean}) (Gy)</td>
<td>50.2 ± 0.4</td>
<td>49.7 ± 0.3</td>
</tr>
<tr>
<td>PTV(_{70})</td>
<td>V(_{47.5})%</td>
<td>97.8 ± 2.2</td>
<td>97.8 ± 2.4</td>
</tr>
<tr>
<td></td>
<td>V(_{50})%</td>
<td>68.2 ± 9.7</td>
<td>75.5 ± 15.0</td>
</tr>
<tr>
<td></td>
<td>V(_{52.5})%</td>
<td>19.1 ± 11.2</td>
<td>18.2 ± 11.3</td>
</tr>
<tr>
<td></td>
<td>D(_\text{mean}) (Gy)</td>
<td>50.9 ± 0.5</td>
<td>51.1 ± 0.7</td>
</tr>
<tr>
<td>C(_\text{RTGOG})</td>
<td>1.69 ± 0.19</td>
<td>1.59 ± 0.16</td>
<td>0.021</td>
</tr>
<tr>
<td>CN</td>
<td>0.48 ± 0.05</td>
<td>0.47 ± 0.05</td>
<td>0.255</td>
</tr>
<tr>
<td>HI</td>
<td>0.86 ± 0.03</td>
<td>0.84 ± 0.03</td>
<td>0.006</td>
</tr>
<tr>
<td>HI(_\text{Wu})</td>
<td>0.20 ± 0.04</td>
<td>0.23 ± 0.03</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Parotids

<table>
<thead>
<tr>
<th></th>
<th>Left</th>
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<th>Right</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>D(_\text{mean}) (Gy)</td>
<td>46.6 ± 9.4</td>
<td>48.4 ± 8.3</td>
<td>0.184</td>
</tr>
<tr>
<td></td>
<td>D(_\text{mean}) (Gy)</td>
<td>48.2 ± 9.9</td>
<td>49.5 ± 8.2</td>
<td>0.345</td>
</tr>
</tbody>
</table>

For the PTV\(_{70}\) and for the parotids, there was no significant difference between the techniques. The
homogeneity was better with the OPFT, but the conformity depended on the index employed. When we used the RTOG index, the conformity was better with the OPFT, and when we used the conformation number, the difference was not significant.

In Table 7 the parameters for all 33 patients are given. Here as well, the parameters referring to PTV50 were significantly greater in the OPFT. Concerning the PTVboost the differences were not significant, with the exception of V50. Again like in the DR case, the two indices describing the conformity showed different significance – the RTOG index was significantly better with OPFT, but the conformation number was not. The homogeneity was better with the OPFT, and the mean doses to the parotids were significantly smaller.

Table 7. Dosimetric comparison of the techniques for all patients

<table>
<thead>
<tr>
<th></th>
<th>Mean values ± SD</th>
<th>OPFT</th>
<th>EPT</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTV50</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V47.5 (%)</td>
<td>90.6 ± 4.4</td>
<td>87.4 ± 3.8</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>V50 (%)</td>
<td>62.0 ± 10.9</td>
<td>58.0 ± 8.2</td>
<td>0.025</td>
<td></td>
</tr>
<tr>
<td>V52.5 (%)</td>
<td>13.8 ± 6.4</td>
<td>9.8 ± 4.5</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>Dmean (Gy)</td>
<td>50.3 ± 0.6</td>
<td>50.0 ± 0.5</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>PTVboost</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V47.5 (%)</td>
<td>96.7 ± 2.8</td>
<td>97.2 ± 2.4</td>
<td>0.094</td>
<td></td>
</tr>
<tr>
<td>V50 (%)</td>
<td>75.4 ± 12.7</td>
<td>80.9 ± 12.1</td>
<td>0.010</td>
<td></td>
</tr>
<tr>
<td>V52.5 (%)</td>
<td>27.9 ± 16.7</td>
<td>24.5 ± 12.7</td>
<td>0.118</td>
<td></td>
</tr>
<tr>
<td>Dmean (Gy)</td>
<td>51.2 ± 0.7</td>
<td>51.3 ± 0.6</td>
<td>0.802</td>
<td></td>
</tr>
<tr>
<td>CIRTOG</td>
<td>1.79 ± 0.23</td>
<td>1.72 ± 0.22</td>
<td>0.017</td>
<td></td>
</tr>
<tr>
<td>CN</td>
<td>0.46 ± 0.05</td>
<td>0.45 ± 0.06</td>
<td>0.150</td>
<td></td>
</tr>
<tr>
<td>HI</td>
<td>0.86 ± 0.02</td>
<td>0.85 ± 0.03</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>HI_wu</td>
<td>0.20 ± 0.04</td>
<td>0.22 ± 0.03</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Parotids</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dleft mean (Gy)</td>
<td>42.0 ± 9.2</td>
<td>44.4 ± 7.8</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Dright mean (Gy)</td>
<td>42.6 ± 9.1</td>
<td>44.3 ± 7.9</td>
<td>0.004</td>
<td></td>
</tr>
</tbody>
</table>

4. CONCLUSION

As we can see from the presented results, for the patients with PRNR, DR and when all the patients are considered as one group, the OPFT showed better coverage of PTV50. For the patients with PRPR the techniques were similar.

With exception of the V50 for the patients with PRNR and the entire group of patients, the coverage of the high risk volume did not differ significantly.

The conformity depended on the index used. When the RTOG index was used, the conformity of the OPFT was superior for the patients receiving DR and the entire group of patients. But when conformation number was used, the difference was not significant in any of the groups.

The OPFT was superior in regard to homogeneity in all 4 groups of patients.

As for the parotids, they were irradiated less in OPFT for the patients with PRNR and for the entire group of patients. In the other two groups, the doses to the parotids did not differ significantly.

So, we conclude that the OPFT gave somewhat better dosimetric results for patients with PRNR and DR and for the entire group of patients. For patients with PRPR the techniques were similar.

Bearing in mind that OPFT eliminates certain dosimetric and practical problems that are present in the EPT, like the field matching and the process of molding the individual blocks for the electron fields, we believe that these results justify going to the next step in introducing the OPFT as standard protocol at our institution - a clinical study evaluating both techniques from a clinical point of view.

5. REFERENCES


DETERMINING THE EFFICIENCY OF A COMMERCIAL BELLY BOARD DEVICE IN REDUCING SMALL BOWEL VOLUME IN RECTAL CANCER PATIENTS

Dushko Lukarski¹, Sonja Petkovska¹, Natalija Angelovska¹, Biljana Grozdanovska¹, Nenad Mitrevski¹,

¹ University Clinic for Radiotherapy and Oncology, Vodnjanska 17, Skopje, R. Macedonia, duskol@yahoo.com.

Abstract – The purpose of this treatment planning study was to evaluate the efficiency of a commercial belly board device in reducing the irradiated volume of the small bowel.

In this study 10 patients with rectal carcinoma receiving postoperative radiotherapy were included. For each of them we made two computer tomography series in prone position. In the first one the patients were lying on the flat table top, and in the second one they were lying on the belly board device which is under investigation. On both series we calculated and optimized plans according to the standing protocol of our department. From the dose-volume histograms of these plans we compared the volumes of the small bowel irradiated to three dose levels – 15, 30 and 45 Gy.

The results showed that the absolute irradiated volumes were significantly smaller in the plans with the belly board device.

Based on these results we believe that the employment of this belly board device will reduce the acute and late small bowel toxicity. This should be verified with a clinical study.

Keywords – belly board, rectal cancer, small bowel.

1. INTRODUCTION

Radiotherapy, alone or in combination with chemotherapy, plays a very significant role in the treatment of rectal cancer. The most important organ at risk (OAR) in the pelvic irradiation, often limiting the treatment, is the small bowel. Several studies [1, 2, 3] show that both acute and late small bowel toxicity is influenced by the volume of the small bowel that is irradiated. Various methods are devised for reducing that volume, both surgical and nonsurgical. Some of the surgical methods include placement of permanent silastic prosthesis, insertion of an absorbable synthetic mesh or omental sling, retroversion of the uterus, and reperitonealization of the pelvic floor. From the nonsurgical methods, the most common are the bladder distension method [4, 5] and employment of a belly board device.

This treatment planning study was intended for verification of one such commercially available belly board device, which our institution has obtained - AIO Bellyboard & Pelvic by the Orfit Industries (Fig. 1).

2. MATERIALS AND METHODS

2.1. Patient population and contouring

A total of 10 patients receiving postoperative radiotherapy were included in this study. In the whole number of patients, an overall stage II was present in 4 patients (40%), another 4 patients (40%) had an overall stage II, while the remaining 2 patients (%) were presented with a recurrent tumor.

Target volumes and OAR were delineated in all axial CT slices according to the recommendations of the RTOG and the ICRU respectively.

The target volumes were defined on the basis of the full bladder scan. The CTV included the macroscopic tumor, rectum, internal, common iliac and presacral LNs. The upper border was at level L5-S1. The posterior and lateral margins of CTV extend to lateral pelvic sidewall musculature or, where absent, the bone. Anteriorly, CTV was extended 1 cm into

![Fig.1 - The belly board device under investigation](image)
Proceedings of the Second Conference on Medical Physics and Biomedical Engineering

the posterior bladder, to account for day-to-day variation in bladder position. Also in the mid pelvis we included at least the posterior portion of the internal obturator vessels (which lie between the external and internal iliacs in the mid pelvis).

The volume PTV was outlined as the CTV with 1 cm margin in all directions. The following OAR were delineated: bladder and small bowel. The small bowel (SB) structure consists of the following: small and large bowel as a whole peritoneal cavity except for LNs, muscles, and OAR other than the SB. The upper border of SB was 1 cm above the PTV.

2.2. Description of the treatment technique

For each patient 2 CT series in prone position were made, with slice thickness of 5 mm. In the first CT series the patient was lying on the flat table top and in the second one he was placed on the belly board. All patients were irradiated without the belly board, according to the standing protocol of our institution.

The treatment planning was conducted using the Eclipse Version 7.3.10, a commercial 3-D treatment planning system manufactured by Varian Medical Systems.

The standing irradiation protocol for postoperative radiotherapy of rectal cancer at our department is irradiation of the PTV by 3 isocentric fields – one dorsal and two lateral photon fields with dynamic wedges (Varian’s Enhanced Dynamic Wedge 60°). The beam quality of the dorsal field is 6MV and that of the lateral fields is 15MV. Roughly one half of the dose is delivered by the dorsal field and the other half by the lateral fields, whose weights are similar. The fractionation scheme is 28 fractions, 1.8 Gy each.

The isocenters of the two plans were chosen in such a manner that the shielded part of the small bowel in the beam’s eye view of both plans was roughly the same. In such a way we were trying to make the plans as similar as possible, in order to exclude the influence of the treatment planning process on the irradiated volume of the small bowel and to evaluate only the influence of the belly board.

2.3. Evaluation and analysis

For each patient we analyzed the dose volume histogram (DVH) for both plans. The focus of the analysis was the small bowel [6-11]. We compared the volumes of the small bowel receiving 15, 30 and 45 Gy both in cubic centimeters and as a percentage of the contoured volume.

In the analysis we compared the means of the respective volumes using the non-parametric Wilcoxon exact signed rank test. Statistical significance was assumed at the level of $p \leq 0.05$.

3. RESULTS AND DISCUSSION

In Table 1 the comparison of the plans with and without belly board is given. We compared the means of the PTVs, the volumes of the SB ($V_{\text{total}}$) and the volumes of the SB receiving 15, 30 and 45 Gy ($V_{15\text{Gy}}$, $V_{30\text{Gy}}$ and $V_{45\text{Gy}}$ respectively) both in cubic centimeters and as a percentage of the total volume. The $p$ value of the corresponding comparison is given in the last column.

<table>
<thead>
<tr>
<th></th>
<th>Without BB</th>
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<tr>
<td>PTV (cm$^3$)</td>
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<td>371 ± 172</td>
<td>0.022</td>
</tr>
<tr>
<td>$V_{45\text{Gy}}$ (cm$^3$)</td>
<td>329 ± 130</td>
<td>275 ± 149</td>
<td>0.007</td>
</tr>
<tr>
<td>$V_{15\text{Gy}}$ (%)</td>
<td>88.8 ± 4.0</td>
<td>87.0 ± 10.4</td>
<td>0.721</td>
</tr>
<tr>
<td>$V_{30\text{Gy}}$ (%)</td>
<td>60.8 ± 12.3</td>
<td>62.6 ± 14.0</td>
<td>0.647</td>
</tr>
<tr>
<td>$V_{45\text{Gy}}$ (%)</td>
<td>45.8 ± 11.0</td>
<td>45.7 ± 13.1</td>
<td>0.959</td>
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On Figure 1 we give typical DVHs for the SB of a patient.

![Dose-volume histogram comparison of the small bowel with and without the belly board device](image-url)

As presented in the table, the difference between the planning target volumes was not significant. Also, the difference between the total contoured volumes of the small bowel was not statistically significant.

When we compared the volumes of the SB as an absolute value (in cubic centimeters), for all three dose levels under investigation (15, 30 and 45 Gy) the plan with the belly board showed significantly smaller volumes irradiated. This was also evident from the dose volume histograms for different patients.

However, as a percentage of the total volume, there was no statistically significant difference in the volumes receiving 15, 30 or 45 Gy.

Since the literature suggests that the important parameter for prediction of both acute and late small bowel toxicity is the absolute volume of the small bowel, to account for day-to-day variation in bladder position. Also in the mid pelvis we included at least the posterior portion of the internal obturator vessels (which lie between the external and internal iliacs in the mid pelvis).

The volume PTV was outlined as the CTV with 1 cm margin in all directions. The following OAR were delineated: bladder and small bowel. The small bowel (SB) structure consists of the following: small and large bowel as a whole peritoneal cavity except for LNs, muscles, and OAR other than the SB. The upper border of SB was 1 cm above the PTV.

2.2. Description of the treatment technique

For each patient 2 CT series in prone position were made, with slice thickness of 5 mm. In the first CT series the patient was lying on the flat table top and in the second one he was placed on the belly board. All patients were irradiated without the belly board, according to the standing protocol of our institution.

The treatment planning was conducted using the Eclipse Version 7.3.10, a commercial 3-D treatment planning system manufactured by Varian Medical Systems.

The standing irradiation protocol for postoperative radiotherapy of rectal cancer at our department is irradiation of the PTV by 3 isocentric fields – one dorsal and two lateral photon fields with dynamic wedges (Varian’s Enhanced Dynamic Wedge 60°). The beam quality of the dorsal field is 6MV and that of the lateral fields is 15MV. Roughly one half of the dose is delivered by the dorsal field and the other half by the lateral fields, whose weights are similar. The fractionation scheme is 28 fractions, 1.8 Gy each.

The isocenters of the two plans were chosen in such a manner that the shielded part of the small bowel in the beam’s eye view of both plans was roughly the same. In such a way we were trying to make the plans as similar as possible, in order to exclude the influence of the treatment planning process on the irradiated volume of the small bowel and to evaluate only the influence of the belly board.

2.3. Evaluation and analysis

For each patient we analyzed the dose volume histogram (DVH) for both plans. The focus of the analysis was the small bowel [6-11]. We compared the volumes of the small bowel receiving 15, 30 and 45 Gy both in cubic centimeters and as a percentage of the contoured volume.

In the analysis we compared the means of the respective volumes using the non-parametric Wilcoxon exact signed rank test. Statistical significance was assumed at the level of $p \leq 0.05$.

3. RESULTS AND DISCUSSION

In Table 1 the comparison of the plans with and without belly board is given. We compared the means of the PTVs, the volumes of the SB ($V_{\text{total}}$) and the volumes of the SB receiving 15, 30 and 45 Gy ($V_{15\text{Gy}}$, $V_{30\text{Gy}}$ and $V_{45\text{Gy}}$ respectively) both in cubic centimeters and as a percentage of the total volume. The $p$ value of the corresponding comparison is given in the last column.

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However, as a percentage of the total volume, there was no statistically significant difference in the volumes receiving 15, 30 or 45 Gy.

Since the literature suggests that the important parameter for prediction of both acute and late small bowel toxicity is the absolute volume of the small
bowel irradiated, we would conclude that the usage of the belly board device would reduce this volume, and thus, reduce the risk of small bowel toxicity.

4. CONCLUSION

The results of this treatment planning study showed that by employment of this particular commercial belly board device we can reduce the absolute irradiated volume of the small bowel. Since the literature shows that both the acute and the late toxicity depend on this absolute irradiated volume, we would recommend a clinical study to compare the toxicity for two series of patients, one with and one without the belly board device.

5. REFERENCES


TRANSMISSION COMPARISON FOR TWO DIFFERENT ELECTRON BLOCK MATERIALS

Sonja Petkovska¹, Dushko Lukarski¹, Margarita Ginovska²

¹ University Clinic for Radiotherapy and Oncology, Vodnjanska 17 Skopje, R. Macedonia, pet.sonja@gmail.com
² Faculty of Electrical Engineering and Information Technologies, Ss Cyril and Metodius University, Skopje, R. Macedonia

Abstract – The purpose of this work is to compare electron beam transmission, under two different block materials. The first one, cerrobend, consists of 10% cadmium and the second one is cadmium free. Percentage depth doses for open and block fields for all electron energies are measured. Measurements were performed with a plan-parallel ionization chamber over a range of depth from water surface to a depth of 160mm. The fields were defined using a 15x15 electron applicator mounted on linear accelerator. Depth dose curves beyond two alloys are matched and compared. Regarding the results, the percentage depth doses behind blocks correspond very well. The difference between the two alloy curves does not exceed 0.12%. The conclusion of the article is that a coincidence in transmission is acceptable.

Keywords – cerrobend, block material, transmission

1. INTRODUCTION

As a result of the photon behavior, the external beam radiotherapy (EBRT) is in some way limited by the inability to deliver adequate doses of irradiation, because of the dose tolerance limits of organ at risk (small bowel, spinal cord, kidney, lenses etc). In treating shallow tumors where a rapid drop off is desired beyond the depth of the tumor (e.g. head&neck lymph nodes over spinal cord, chestwall, skin cancers, other superficial tumors) it is highly recommended to use electron beams. Electrons have an abrupt fall off. They provide a high dose delivered close to the surface and a minimal dose delivered to the deep tissues. Because of their nature, there are some limitations (constraints) in their using such as: the field should always be perpendicular to the beam; dose goes to areas beyond geometrical field; the lower electron isodose lines bulge out below the surface- ballooning or mushrooming [1].

The electron beams can be delivered with a range of applicator sizes and field apertures (cut-outs), depending on the volume which should be treated. The shielding material used in our hospital for modeling blocks was cadmium and lead based shielding alloy (cerrobend). Cerrobend blocks are widely used to protect normal tissues and its characteristics are very well known [2]. Cadmium has been recognized as a source of environmental pollution and a poisonous cadmium gas is emitted during fabrication of the material into custom blocks. However, the potential for exposure to hazardous levels is extremely low if the recommended safe practices are followed, cadmium-free shielding alloy is decided to be used. The alloy, here referred as Rossen, same as the other Cd-free alloys contains a higher concentration of lead and melt at a higher temperature [3, 4].

In this work we compare transmission when an electron beam passes through selected alloys.

2. MATERIALS AND METHODS

Available electron energies are: 4MeV, 6MeV, 9MeV, 12MeV, 16MeV and 20MeV. Electron Pencil Beam Algorithm needs measured dose distribution obtain through open and fully blocked field for reference applicator.

Firstly, we deal with Lipowitz's metal, also called cerrobend alloy, whose melting point is 70 °C. It has a composition of 50% bismuth, 26.7% lead, 13.3% tin and 10% cadmium. Second one is cadmium free alloy, called Rossen, which consists of 0.3% cadmium. Its melting point is 106 °C. Full blocks (for applicator 15) from the two alloys are prepared in the mold-room.

Using a PPC-40 plan-parallel ionization chamber, a Blue water phantom and a 15x15 electron applicator mounted on Varian clinic, we measured the...
percentage depth doses for open and block fields, for all electron energies. OmniPro software allows us to see the depth dose curves, match them and compare them.

3. RESULTS

Depth dose curves comparison for all available electron energies is performed. As it is presented in other studies [5], the maximum dose under a blocked electron beam (for both alloys) occurs on the central axis closer to the surface than it does for the open beam. To be able to interpret the results of the transmission differences, we should know the depth dose distribution for open field (Table 1) and the block transmission factors for available electron energies (Table 2).

Table 1. Depths (mm) in water for selected open field percentage doses

<table>
<thead>
<tr>
<th>Dose (%)</th>
<th>20</th>
<th>10</th>
<th>5</th>
<th>2</th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
<td>d 4MeV</td>
<td>14.3</td>
<td>15.4</td>
<td>16.2</td>
<td>17.0</td>
<td>17.4</td>
</tr>
<tr>
<td>d 6MeV</td>
<td>26</td>
<td>27.8</td>
<td>29.2</td>
<td>30.7</td>
<td>31.7</td>
</tr>
<tr>
<td>d 9MeV</td>
<td>39.5</td>
<td>42</td>
<td>43.9</td>
<td>46.3</td>
<td>48.5</td>
</tr>
<tr>
<td>d 12MeV</td>
<td>55.1</td>
<td>58.6</td>
<td>61.4</td>
<td>66.3</td>
<td></td>
</tr>
<tr>
<td>d16MeV</td>
<td>73.8</td>
<td>78.7</td>
<td>83.5</td>
<td>94</td>
<td></td>
</tr>
<tr>
<td>d 20MeV</td>
<td>94.2</td>
<td>100.8</td>
<td>112</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Transmission factors for electron beams

<table>
<thead>
<tr>
<th>Energy (MeV)</th>
<th>4</th>
<th>6</th>
<th>9</th>
<th>12</th>
<th>16</th>
<th>20</th>
</tr>
</thead>
<tbody>
<tr>
<td>T (%)</td>
<td>0.2</td>
<td>0.4</td>
<td>0.9</td>
<td>2.2</td>
<td>4.2</td>
<td>7.4</td>
</tr>
</tbody>
</table>

The electron beam transmissions under blocks made from different alloys, are presented through percentage depth doses. The percentage depth dose differences are converted into real dose differences using a transmission factor. Results are as it follows.

On the figures below, the red curve represents the cerrobend alloy and the green curve is the new alloy (Cd-free). The transmission curves are normalized to 100% (Dmax=100%). In reality this corresponds to transmission of 0.2%; 0.4%; 0.9%; 2.2%; 4.2% and 7.4% respectively for energies from 4MeV to 20MeV (Tab 2). Comparisons show highest discrepancies for 4MeV electron energy. This OmniPro graph is presented below (Fig. 1).

Fig. 1 – 4 MeV percentage depth dose differences

Table 3. 4 MeV percentage depth dose differences

<table>
<thead>
<tr>
<th>d(mm)</th>
<th>2.7</th>
<th>6.4</th>
<th>15</th>
<th>22</th>
</tr>
</thead>
<tbody>
<tr>
<td>Δ</td>
<td>-5.4</td>
<td>-5</td>
<td>4.3</td>
<td>-9.5</td>
</tr>
<tr>
<td>Δ*T</td>
<td>-0.011</td>
<td>-0.01</td>
<td>0.009</td>
<td>-0.019</td>
</tr>
</tbody>
</table>

where, \( Δ(\%) = D_{\text{Rossen}}(\%) - D_{\text{Cerrobend}}(\%) \)  

The transmitted dose difference goes up to 9.5%, but even that, the real dose difference is less than 0.02%.

For the rest of the electron energies, the results presented below (Table 3) show good adjustment between block transmissions on selected depths.

Table 4. Percentage depth dose differences

<table>
<thead>
<tr>
<th>d(mm)</th>
<th>10</th>
<th>20</th>
<th>40</th>
<th>60</th>
</tr>
</thead>
<tbody>
<tr>
<td>Δ 6MeV</td>
<td>-1.7</td>
<td>-2.3</td>
<td>1.5</td>
<td>2.5</td>
</tr>
<tr>
<td>Δ*T</td>
<td>0.007</td>
<td>0.009</td>
<td>0.006</td>
<td>0.01</td>
</tr>
<tr>
<td>Δ 9MeV</td>
<td>-0.3</td>
<td>-0.6</td>
<td>-1.2</td>
<td>0.3</td>
</tr>
<tr>
<td>Δ*T</td>
<td>0.003</td>
<td>0.005</td>
<td>0.011</td>
<td>0.003</td>
</tr>
<tr>
<td>Δ 12MeV</td>
<td>-0.9</td>
<td>-1.1</td>
<td>-1.8</td>
<td>-1</td>
</tr>
<tr>
<td>Δ*T</td>
<td>-0.02</td>
<td>-0.024</td>
<td>-0.04</td>
<td>-0.022</td>
</tr>
<tr>
<td>Δ 16MeV</td>
<td>0.1</td>
<td>-0.5</td>
<td>-0.2</td>
<td>-0.5</td>
</tr>
<tr>
<td>Δ*T</td>
<td>-0.004</td>
<td>-0.021</td>
<td>0.008</td>
<td>-0.021</td>
</tr>
<tr>
<td>Δ 20MeV</td>
<td>-1.5</td>
<td>-1.5</td>
<td>-1.4</td>
<td>-1.4</td>
</tr>
<tr>
<td>Δ*T</td>
<td>-0.111</td>
<td>-0.111</td>
<td>-0.104</td>
<td>-0.104</td>
</tr>
</tbody>
</table>

The first line in each row shows differences when the maximal values of the transmission curves are normalized to 100%. The second line shows these differences when corresponded transmission factors are taken into account.

4. CONCLUSION

Regarding the results, the percentage depth doses behind blocks correspond very well. The difference

Fig. 2 – 9 MeV percentage depth dose differences

Coincidences between two curves are much better for the rest electron energies. Almost ideal coordination in transmission through two blocks is found for the most frequently used electron energy (Fig. 2)
between the two alloy curves does not exceed 0.12%. As the coincidence between transmissions is obviously acceptable, the cerrobend alloy can be replaced with a new one. We should take into account that the cerrobend replacement does not mean that the problem with the alloy will disappear. The Cadmium-free alloy has a little bit lower transmission than the Lipowitz’s metal, primarily due to the higher content of lead and bismuth, and it also has a higher melting point. While cadmium-free alloy was designed to eliminate cadmium from the workplace, it does not eliminate the potential problem of lead. Based on all current studies and published reports, it would appear that the alloy fumes do not present a real problem when following certain safety procedures. The potential problem of cadmium is minimized to the extent that it is difficult to make a valid argument supporting the use of a higher temperature, especially since the elevated pouring temperature creates a greater potential for serious burns.

A good solution for the future is a new material with higher attenuation, easy to fabricate and friendly to the environment [6, 7, 8], used as a substitute of lead.

5. REFERENCES


CONFORMITY INDEX FOR BRAIN CANCER PATIENTS

Sonja Petkovska¹, Cveta Tolevska¹, Slavica Kraleva¹, Elena Petreska²

¹ University Clinic for Radiotherapy and Oncology, Vodnjanska 17, Skopje, R. Macedonia, pet.sonja@gmail.com, skraleva@gmail.com
² City University of New York, Menheeten, New York, USA, elena_petreska@yahoo.com

Abstract – The purpose of this study is to present the level of conformity achieved by using 3D conformal radiotherapy for brain cancer patients. Conformity index is a helpful quantitative tool for assessing (evaluating) the quality of a treatment plan. Treatment plans made for ninety patients with brain tumor are worked on this paper. The patients are in supine position and immobilized with thermoplastic masks for the head. Computed tomography data sets with 5 mm scan thickness are used to create a 3D image. All structures of interest are contoured. In order to obtain an optimal dose distribution, treatment fields are fit around target volume with set-up margins of 7mm in each direction.

The conformity index values are between 1.21 and 2.04. Value of 1.8 is exceeded in eighteen cases; nine of them are bigger than 1.9 and only three of them are above 2. The target volume for each of these extreme CI values is ideal covered (between 95% and 105% of the prescribed dose). The most acceptable conformity index value in this paper belongs to the plan with the lowest minimal dose (84.7%).

It can be concluded that conformity index is necessary but not sufficient factor for assessing radiation treatment plan conformity. To be able to estimate the acceptability of some treatment plan in daily practice, additional information as minimal, maximal and mean dose into target volume, as well as health tissues coverage must be taken into account.

Keywords – treatment planning, brain cancer, 3D conformal radiotherapy, conformity index

1. INTRODUCTION

Three-dimensional conformal radiation therapy (3DCRT) is a high-precision type of radiotherapy, regarding volumes definition (target and organs at risks), patient immobilization, and treatment delivery. The use of multileaf collimator (MLC) gives a possibility of shaping the isodose surfaces around volume of interest (i.e., the planning target volume) in all three dimensions. This enables to approach the first principle in radiotherapy: increase the dose in the tumor as much as possible and minimize the irradiated normal tissue volumes at the same time. Quantification of the three dimensional dose distribution is represented in the form of dose–volume histograms (DVH). By using DVH, it became possible to define the maximal, minimal, mean, and modal dose values delivered to each volume of interest. It also allows comparison of DVHs for the same structures into two (or more) different plans for the same patient. We can easily choose between several options ensuring the same tumor coverage and the same protection of some critical organs in favor of the option that most effectively protects the other organ at risk. But, all healthy tissues cannot be taken into account, because of the difficulties of delineation and absence of sufficient data concerning the tolerance of these tissues to the absolute dose received, or the magnitude of the volume irradiated [1].

In spite of the facts above, it is not easy to determine the level of conformity. Analysis of each parameter relevant for the treatment (e.g. clinical, radiologic, radiobiologic geometric, dosimetric) is very complex and time-consuming. An additional tool that integrates all these data and quantitatively assess the quality of a treatment option is the conformity index.

The conformity index was first proposed in 1993 by the Radiation Therapy Oncology Group (RTOG) and described in Report 62 of the International Commission on Radiation Units and Measurements (ICRU). It is presented as a relation between the volume of the reference dose (Vn) and the target volume(TV).

\[ \text{Conformity index}_{\text{RTOG}} = \frac{V_n}{TV} \]  

According to the RTOG guidelines, ranges of conformity index values have been defined to determine the quality of conformation. If the conformity index is situated between 1 and 2, the treatment is considered to comply with the treatment
plan; an index between 2 and 2.5, or 0.9 and 1, is considered to be a minor violation, and when the index value is less than 0.9 or exceeds 2.5, the protocol violation is considered to be major, but may nevertheless be considered to be acceptable [2].

CI=1 is an ideal, theoretical value but even if it is a real one, it doesn’t mean that high level of conformity is achieved. Volume of reference dose could be shifted out of target volume with perfect mathematical corresponding. Obviously to be able to assess conformity in daily practice, additional parameters as minimal isodose surrounded target volume, or maximal dose and mean dose into target volume, must be determined.

In this paper we will evaluate dose distribution, conformity index and its relation to minimal dose.

2. MATERIALS AND METHODS

Ninety brain cancer patients (Glioblastomas-50, Astrocytomas-20, oligodendrogliomas-20), selected consecutively from our clinical database in the period of one year 2007, treated on the same linear accelerator, have been evaluated retrospectively. Prescribed dose for all patients is 60Gy in 30 fractions, 1 fraction per day, 5 days weekly.

Treatment plans were created according to the three-dimensional conformal radiotherapy [3D-CRT] on computed tomography (CT) data sets of above brain tumor patients. The CT scan should start at the top of the cranial vertex and down to the neck to encompass the entire cranial contents and the head. CT scan thickness is 0.5 cm through the whole scanning region. The patients are in supine position, immobilized with thermoplastic head&neck mask. CT isocenter is marked on the mask.

The gross tumor volume (GTV), situated in the parietal or frontal lobe and outlined on all CT slices in which the structure exist, has a margin of 1cm to define clinical target volume (CTV). Planning target volume (PTV) is 1cm around the CTV. The brain stem and both lenses are delineated as organs at risk (OAR). Because of the anatomical barriers or OAR that are not infiltrated, in some cases PTV is corrected.

The aim of the planning is to cover the PTV with at least 95% of the prescribed dose. Treatment plans are made with 3 fields, left, right and vertex (couch rtn 90ø, gantry angle depended on the tumor and eyes position is between 20ø and 70ø). The planning fields are fit around the PTV with setup margine of 7mm. The MLC is always adjusted to the planning field. Enhanced dynamic wedges are also available. If the CT isocenter was changed during the planning, it is marked on the mask additionally (before irradiation treatment starts) using movable lasers mounted on CT couch.

3. RESULTS

Dose distribution

ICRU protocol requires a minimal dose of 95% (which is also reference dose in this paper) and a maximal dose of 107% of prescribed dose into target volume (PTV in this paper). Most of the PTVs (more than 50%) are close to the eyes or body surface, so a minimal dose of 95% into PTV is very difficult to achieve. The lowest value of the minimal dose is 84.7%, but the mean dose is not less than 99.2% in all cases (Table 1).

<table>
<thead>
<tr>
<th></th>
<th>Dmin (%)</th>
<th>Dmax (%)</th>
<th>Dmean (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>from</td>
<td>84.7</td>
<td>103.4</td>
<td>99.2</td>
</tr>
<tr>
<td>to</td>
<td>96.5</td>
<td>108.7</td>
<td>102.1</td>
</tr>
<tr>
<td>mean</td>
<td>92.9</td>
<td>105.6</td>
<td>100.6</td>
</tr>
</tbody>
</table>

The minimal doses of the invested patients are presented below (Fig. 1). In 10% of them the minimal dose is less than 90%.

As it is shown below (Fig 3) there are 11 cases where the maximal dose exceeds 107%, but is less than 109% and situated always in PTV.

Conformity index

According to the RTOG guidelines, a conformity index value less than 1 means that not whole PTV is covered by reference dose. Values above 2 point that even coverage of PTV is acceptable; health tissue included into the reference dose volume is not negligible.

In the results presented below (Fig. 3), it can be seen that there is not any conformity index value less than
1, which means that the reference dose volume (\(V_{95}\)) is always bigger than the target volume (PTV). Conformity index values are between 1.21 and 2.04, \(C_{\text{mean}}\) is 1.68. Most of the values (eighty patient plans or 90%) are situated in the region between 1.4 and 1.9. Value 1.8 is exceeded in eighteen cases; nine of them are bigger than 1.9 and only three of them are above 2.

Even if we select a subgroup with perfect PTV coverage, \(95\%<D_{\text{PTV}}<106\%\), \(CI\) varies between 1.46 and 2.01, 1.67 in average, and there is also no dose dependency.

4. CONCLUSION

From the results we can note that: \(CI\) for brain cancer patients worked on this paper is in the frame of RTOG recommendations; it is above 1.46 even in the case of the best PTV coverage; and it does not correspond to the minimal dose. The intention of the pretreatment planning should be lower \(CI\) than presented value, but decreasing of \(CI\) (e.g. \(V_{95\%}\)) leads to underdosage of the target volume.

It can be concluded that conformity index is necessary tool for evaluation of treatment plan adequacy, but it is not sufficient factor for assessing radiation treatment plan optimality. To be able to estimate the acceptability of some treatment plan in daily practice, additional information as minimal, maximal and mean dose into target volume, as well as health tissues coverage must be taken into account. Together with other evaluation tools (DVH, visual isodose inspection e.t.c.) it should be used for determining the level of conformity.

In the future we should try to improve the treatment planning modalities, to be able to decrease the volume of the reference dose (\(V_{95\%}\)), and at the same time achieve a target volume (PTV) included into the reference dose volume.

5. REFERENCES


VALIDITY OF PRV MARGINS AROUND LUNG AND HEART DURING LEFT BREAST IRRADIATION

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Abstract – Purpose: Planning organ at risk volumes (PRV) has a minor use in radiotherapy treatment planning. During left breast irradiation two critical volumes are of special importance – the lung and the heart. The aim of this study was to evaluate the changes in volume doses after adding appropriate margins around these organs at risk and compare them with the effect that the systematic positioning error has on the volume doses.

Methods: Treatment plans for 44 patients with left breast cancer were analyzed. Two changes for each plan were made, and dose-volume histogram values for hearts and lungs volumes were recorded. In the first case margins of 5 mm to hearts and lungs were added. Volumes that were enclosed by 30% isodose for hearts and volumes that were enclosed by 20% isodose of lungs were recorded. In the second case plans were made with a systematic error of 5 mm employed, depicting a translation of isocenter posterior and to the right. In this second case, monitor units were taken from the original plan. The critical volumes for hearts and lungs were recorded as in the first case.

Results: Our policy for breast cancer irradiation demands that the lung volume receiving 20 Gy should be kept under 25% of the whole left-lung volume, and no more than 10% of the heart volume should receive more than 30 Gy. The first case simulation showed that 23% of the patients have a heart overdose while 11% of them have a lung overdose according to the criteria above. Simulation of the second kind showed that the systematic error in isocenter positioning of 5 mm gives bigger a volume of the heart (in average 0.69% of heart volume) to be enclosed in critical isodose than in PRV case. For the lung the situation was opposite; namely in PRV case the lung volume that is encompassed with critical isodose is greater (in average 1.47% of lung volume) than in a case of displaced isocenter.

Conclusions: Adding PRV margins around the heart and the lung does not give straightforward and unambiguous result for the degree of irradiation of these critical organs. Several organs at risk are overlapping esophagus and this situation restricts the use of the PRV concept. Nevertheless, a method with displaced isocenter can reveal some potential risk of overdosage of these critical structures guiding the planner towards making a new plan in order to lower the dose to the OARs.

Keywords – Organs at risk, planning organ at risk volume, conformal radiotherapy

1. INTRODUCTION

It is well known that for a radiotherapy treatment usually three volumes should be defined. In most cases gross tumor volume (GTV), clinical target volume (CTV) and planning target volume (PTV) should be defined in order to perform a proper radiotherapy. The planning target volume assures us that the CTV will receive predefined percentage of the prescribed dose. This concept works well when the tumor is in question. But, almost always we have some critical healthy structure near the tumor. In that case we should strive to spare that structure from a too high dose in order not to damage it because it can have fatal consequences for the patient. So, similar to the concept of PTV, we should define some margins around the organ at risk (OAR) and make a plan that will satisfy the double criteria: the prescribed dose to be delivered to the PTV and a dose below the tolerance dose could reach the OAR. These margins around the OAR form planning organ at risk volume (PRV). The ICRU Report No. 62 [1] suggests drawing such margins around the organs at risk (OAR) but anyhow the concept of PRV has minor use in the contemporary radiotherapy treatment planning.

The margins of PRV should take into account the motion of the organ at risk and patient setup uncertainties. Unfortunately, ICRU Report 62 does not give any proposals how to draw these margins. During left breast irradiation two critical volumes are of special importance – the lung and the heart. The aim of this study is to compare two simulation
methods which will yield to the changes in the volumes of the OARs that will be encompassed by the certain isodose lines. Comparison is made for the plans with PRV margins added and the plans with displaced isocenter.

2. MATERIALS AND METHODS

Treatment plans for 44 patients with left breast cancer were analyzed. For each plan two cases were considered, changes were made, and dose-volume histogram (DVH) values for the hearts and the lungs were recorded. In the first case, margins of 5 mm around the hearts and the lungs were added. Figure 1 represents a treatment plan depicting critical organs (heart and lung) with and without margins. With the help of the dose-volume histogram tool the volumes that were enclosed by the 30% isodose lines for hearts and the volumes that were enclosed by the 20% isodose lines of lungs were recorded.

In the second case, plans were made with a systematic positioning error of 5 mm employed, which is mainly due to the treatment preparation uncertainties, depicting translation of the isocenter posterior and to the right of the patients. Figure 2 shows a plan with the displaced isocenter. With this translation we are trying to put the critical structures in a position similar to the one that the PRV structures occupy. The treatment plans retain the original monitor units as they were planned for treatment delivery. The critical volumes enclosed by appropriate isodoses for hearts and lungs were recorded as in the first case.

During the recent years several tests for determining random positional errors were performed in our clinic. They reveal that the random errors during the patient’s positioning and treatment are less than a millimeter and they are quite small and negligible compared to the treatment preparation uncertainties. It is supposed that due to the breathing and the heart beating, a motion is included in some degree in the CT scan images and adequately in the 3D reconstruction of the body structures. Because of that we used that: the maximum uncertainty of positions of these OAR might be 5 mm. The PRV are purely margins which will result as a consequence of the systematic errors and the internal organ motion relative to bony structures.

There are only several papers dealing with the PRV matter. In one of them [2] the authors give a proposition on how to determine margins for the PRV construction. They conclude that drawing margins around both serial and parallel OARs can alert the planner or the radiation oncologist to the possibility of high-dose complications in individual treatment plans.

We presume that the volumes of the PRV structures enclosed by the appropriate isodose lines will not be different from the volumes of the critical structures enclosed by the same isodose lines values obtained by isocenter moving. The purpose of this comparison is to quantify the difference between these two types of volumes.

3. RESULTS

When we have a case with a serial structure OAR (such as spinal cord) we can decide easily about the critical dose inspecting the cumulative DVH. In this case any point of the OAR should receive a dose less than the tolerance dose. The only thing we should determine is the margin we should draw to obtain PRV around the OAR and then apply the DVH routine on that PRV. But the heart and the lung are critical structures of different composition. For the heart it is accepted that it is a ‘serial-parallel’ structure. The lung is a parallel structure which means that some small parts of it can receive devastating doses while the function of the organ as a whole will not be obstructed.

Our policy for breast cancer irradiation demands that the lung volume receiving 20 Gy should be kept under 25% of the whole left-lung volume, and no more than 10% of the heart volume should receive more than 30 Gy. The first case simulation (PRV
margins added) showed that 23% of the patients have a heart overdose while 11% of them have a lung overdose according to the criteria above [4]. Simulation of the second kind (isocenter displacement) showed that the systematic error in isocenter positioning of 5 mm gives a bigger volume of the heart (in average 0.69% of the heart volume) to be enclosed with the critical isodose than in the PRV case. For the lung the situation was opposite; namely, in PRV case the lung volume that is encompassed with critical isodose is greater (in average 1.47% of lung volume) than in a case with displaced isocenter.

We performed an unpooled two-sample t-statistic to compare the means of the two types of simulations. The both t-test analysis (for hearts and lung volume means) showed that there is no significant difference in the encompassed OAR volumes for the two simulations. This shows that an ordinary isocenter displacement in appropriate directions can reveal whether we should be concerned about the amount of the heart and the lung volumes endangered by our treatment plan. Making another plan for the new isocenter while leaving another plan parameters unchanged is a straightforward and a quick process. This plan can be used solely for assessment of the OARs endangerment.

Despite this positive simulation, adding PRV margins has some disadvantages. It usually happens that the margin enters another body structure and it spoils the homogeneity of the OAR. For example, adding margins to the lung expands it into the thoracic wall and that means we can not rely on the accuracy of the isodose lines for the whole lung.

Table 1. t-test analysis for the heart volumes (cm³)

<table>
<thead>
<tr>
<th>Mean</th>
<th>Std. Error</th>
<th>t</th>
<th>p-value</th>
<th>Lower 95%</th>
<th>Upper 95%</th>
</tr>
</thead>
<tbody>
<tr>
<td>-4.54</td>
<td>5.98</td>
<td>0.759</td>
<td>0.450</td>
<td>-7.35</td>
<td>16.44</td>
</tr>
</tbody>
</table>

Table 1 shows t-test analysis for the means of heart volumes enclosed by 30% isodose for the both simulations. It can be seen that we can assume that both samples belong to the same population. The same case is for the lung volumes shown in table 2.

Table 2. t-test analysis for the lung volumes (cm³)

<table>
<thead>
<tr>
<th>Mean</th>
<th>Std. Error</th>
<th>t</th>
<th>p-value</th>
<th>Lower 95%</th>
<th>Upper 95%</th>
</tr>
</thead>
<tbody>
<tr>
<td>-20.93</td>
<td>28.82</td>
<td>-0.726</td>
<td>0.470</td>
<td>-78.22</td>
<td>36.37</td>
</tr>
</tbody>
</table>

4. CONCLUSION

Adding PRV margins around heart and lung does not give straightforward and unambiguous result for the
degree of irradiation of these critical organs. Several organs of risk are overlapping esophagus and this situation restricts the use of the PRV concept. Also, the lung protrudes into the thoracic wall and in that way its density is changed. The authors in reference [3] conclude that the concept of PRV for planning of radiotherapy is of limited use and they suggest that some alternative ways should be developed to include geometric uncertainties of OARs in radiotherapy planning. As we have seen that endangered volumes in plans with PRV and plans with a displaced isocenter belong to the same population, an alternative way to estimate dose-volume constraints for the OARs might be to make a plan with the displaced isocenter. It is usually easier during the treatment planning process to make another plan with appropriately displaced isocenter and using DVH tool, the planner can asses the change of the OAR irradiated volume and accordingly can make decision about the appropriateness of the original plan. In a case where the heart or the lung receives excessive dose, the planner or the radiation oncologist can decide to try another plan which will spare the OARs according to the treatment policy of the clinic.

5. REFERENCES


RADIATION PROTECTION REQUIREMENTS FOR MEDICAL APPLICATION OF IONIZING RADIATION IN THE REPUBLIC OF MACEDONIA

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Abstract – In this paper, the regulatory infrastructure in radiation protection in the Republic of Macedonia is presented. The national radiation protection requirements for the medical application of ionizing radiation are reviewed for both occupational exposed persons and patients undergoing a medical treatment with ionizing radiation and their compliance with the international standards is considered. The gaps identified on the national level are presented and steps for overcoming such gaps are analyzed.

Keywords – radiation protection, ionizing radiation, medical exposure

1. INTRODUCTION

Legislative and regulatory framework in radiation protection and safety in the Republic of Macedonia is established with the Law on ionizing radiation protection and safety [1] adopted in 2002 and amended in 2007. This Law [1] establishes a competent authority, the Radiation Safety Directorate (RSD), as an independent governmental institution for carrying out the administrative and professional activities in the field of radiation protection and safety, and nuclear security. The principle functions and activities of the RSD are determined with the Law [1] as following: establishing radiation protection and safety requirements through development of regulations, guides and other acts; licensing practices involving ionizing radiation sources; performing inspections and enforcing the regulatory requirements; maintaining a national register on ionizing radiation sources, occupational exposed persons and nuclear material; establishing intervention levels and undertaking interventions in a case of emergency; establishing institutional and international cooperation on matters within the competence of the RSD etc. Therefore, the radiation protection and safety requirements in different applications of ionizing radiation sources, including the medical application, are to be established and enforced by the RSD.

Pursuant to the Law [1], the Radiation Safety Commission, as an advisory body to the RSD in relation to radiation protection issues, has been established by the director of the RSD consisting of representatives from different institutions determined in Article 5 of the Law [1]. Moreover, under the current legislation, technical services are clearly separated from the regulatory functions and activities of the RSD. Namely, the Law [1] recognizes the Republic Institute of Public Health Protection (now, Institute of Public Health) as a technical service provider to the RSD. However, the RSD is also given the possibility to give authorization (as prescribed in Chapter II-a of the Law [1]) to other technical service providers for performing different technical services that are required for enforcing the Law itself.

2. RADIATION PROTECTION IN MEDICAL APPLICATION OF IONIZING RADIATION

Ionizing radiation sources in the Republic of Macedonia are used in medicine in both diagnostic and therapeutic procedures within different practices: diagnostic and interventional radiology (involving CT’s, mammography units, conventional radiography units, fluoroscopy units, dental X-ray units, angiography units etc.), radiotherapy (involving linear accelerators, ortovoltage unit, Co-60 teletherapy unit, LDR brachytherapy unit with Ir-192) and nuclear medicine (diagnostic and therapeutic with I-125, Tc-99m, I-131 etc.). While performing the practice itself, the main responsibility for ensuring radiation protection is given to the legal entity according to Article 13, paragraph 3 of the Law [1]. But, however, according to Article 17 of the Law [1] each person employed or temporary engaged by the legal entity performing practice involving ionizing radiation is obliged to implement the radiation protection and safety requirements set forth in the
Law [1] and the regulations adopted pursuant to this Law.

According to the Law [1], no legal entity could start a practice involving ionizing radiation (including the medical application of ionizing radiation) unless licensed by the RSD. For that purpose, the legal entity should submit license application to the RSD in accordance with [2] in order to demonstrate the compliance with the regulatory requirements. Verification of the fulfillment of all the regulatory requirements is then done during the control and assessment of the license application and with inspection within the licensing process as prescribed with [2]. No license is needed to be granted by the RSD if the legal entity performs a practice involving ionizing radiation source that is exempted or if the radiation exposure is excluded from regulatory control in accordance with [3].

In addition to the Law [1], the regulations [2] and [4] to [7] adopted pursuant to this Law cover some specific radiation protection requirements for the occupational exposed persons as well as some specific radiation protection requirements in connection to the medical exposure. Furthermore, in reference to the medical application of ionizing radiation, some of the regulations inherited from the Former Yugoslavia are still applicable such as [8], [9] and [10].

2.1. Basic principles of radiation protection


- No license shall be issued by the RSD according to Article 9 of the Law [1] for a practice involving ionizing radiation that is not justified taking into account all the social, economic and other relevant factors;

- Each legal entity performing a practice involving ionizing radiation shall ensure that the occupational protection and safety is to be optimized in accordance with the ALARA principle; and

- The total dose received by any person shall not exceed the dose limits set in [4] taking into account all the exposure pathways and all the sources of exposure with the exception of the doses incurred within the medical exposure.

The optimization of the occupational radiation protection should be described in more details within the Radiation Protection Programme in accordance with [1] and [7] which is in line with the IAEA Basic Safety Standards No. 115 [11] and the Council Directive 96/29 [12]. The legal entity should demonstrate compliance with the above mentioned radiation protection requirements in connection with the occupational radiation exposure within the licensing process. A detailed description on how these requirements are met should be given in the Radiation Protection Programme in accordance with [7]. Some specific requirements in connection with the: suitable and appropriate facilities and equipment; qualifications and training of the persons engaged in work with ionizing radiation; health conditions to be fulfilled by any person engaged in work involving ionizing radiation and the health surveillance as well as specific requirements in connection to the individual monitoring, workplace monitoring and records maintaining are given in [4] to [10] and [13].

2.2 Occupational radiation protection

The legal entity performing a practice involving ionizing radiation, in accordance with Articles 8 and 13 of the Law [1] must, inter alia, ensure:

- Suitable and appropriate facilities and equipment for providing radiation protection;

- Personal protective equipment and monitoring equipment;

- Appropriate qualified and trained personnel;

- Health surveillance for the occupational exposed persons;

- Radiation exposure assessment (through both individual monitoring and workplace monitoring);

- Radiation Protection Programme which contains the Emergency Preparedness Plan and the Quality Assurance and Quality Control Programme;

- Appropriate internal organization and management; and

- Maintaining records in connection with the ionizing radiation sources, occupational exposed persons, radiation protection and safety measures,

which is in line with the IAEA Basic Safety Standards No. 115 [11] and the Council Directive 96/29 [12]. The legal entity should demonstrate compliance with the above mentioned radiation protection requirements in connection with the occupational radiation exposure within the licensing process. A detailed description on how these requirements are met should be given in the Radiation Protection Programme in accordance with [7]. Some specific requirements in connection with the: suitable and appropriate facilities and equipment; qualifications and training of the persons engaged in work with ionizing radiation; health conditions to be fulfilled by any person engaged in work involving ionizing radiation and the health surveillance as well as specific requirements in connection to the individual monitoring, workplace monitoring and records maintaining are given in [4] to [10] and [13].

2.3 Radiation protection for medical exposure

The Law [1] defines the medical exposure as exposure incurred by:

- patients as part of their own diagnostic or therapeutic procedures;

- persons, other than those occupationally exposed, knowingly while voluntarily
helping in the support and comfort of patients; and
- volunteers in programs of biomedical research involving their exposure,
which is in line with the IAEA Basic Safety Standards No. 115 [11].

The principles of justification and optimization are also applicable with regard to the medical exposure and they are introduced in the national legislation in accordance with the IAEA Basic Safety Standards No. 115 [11] and the Council Directive 97/43 [14]. The other relevant requirements in relation to the medical exposure set in [11] and [14] are also applicable in the Republic of Macedonia. Namely, according to the Article 20 of the Law [1], each medical exposure should be justified by weighing out the diagnostic or therapeutic benefits it produces, against the radiation detriment it might cause, taking into account the benefits and the risks of available alternative techniques not involving a medical exposure. Article 21 of the Law [1] gives the legal entity responsibility to ensure that:

- no patient is administered a diagnostic or therapeutic medical exposure, unless the exposure is prescribed by a medical doctor or medical doctor-specialist;
- doctors are assigned the primary tasks and obligations of ensuring an overall patient protection and safety in the prescription of, and during the delivery of, medical exposure;
- medical and paramedical personnel is available as needed (includes either health professionals or professionals that have appropriate professional training) to implement the assigned tasks related to the diagnostic and/or therapeutic procedures prescribed by a medical doctor or medical doctor-specialist;
- calibration, dosimetry and quality assurance under supervision of a medical physicist or specialist in medical nuclear physics, during diagnostic and/or therapeutic application of ionizing radiation (including teletherapy, radionuclide therapy and brachytherapy); and
- training of personnel in line with the Law [1] and regulations adopted pursuant to this Law.

Moreover, Article 2 of [9] specifies the medical doctors that could be entitled for prescription and approval of diagnostic and therapeutic procedure involving ionizing radiation. Within the process of justifying the diagnostic and/or therapeutic procedure involving ionizing radiation, according to Article 3 of [9], the medical doctor entitled for the prescription of the procedure shall individually justify the procedure itself taking into account the illness, the characteristics (age, gender etc.) of the individual undergoing the procedure, health benefit for the individual as well as the possible detrimental effects for both the individual and the population. In addition to this, the medical doctor entitled for approval of the diagnostic and therapeutic procedure involving ionizing radiation, according to Article 6, point 1 of [9] shall determine whether the medical exposure is justified for obtaining the necessary diagnostic information or achieving the needed therapeutic effects taking into account the available alternative techniques which are less risky. The previous diagnostic examinations involving ionizing radiation shall be taken into account with the process of justifying the additional referral of an individual to a procedure involving ionizing radiation where applicable as prescribed in Article 7 of [9]. The medical doctor entitled to approve the medical exposure in accordance with the Article 6, point 3 of [9] is obliged not to allow undergoing diagnostic and therapeutic procedure involving ionizing radiation unless justified. Article 6, point 2 of [9] states that the medical doctor entitled to approve the medical exposure in accordance with the provisions of the same regulation, should determine the conditions for carrying out the procedure so as to ensure that the doses incurred by an individual undergoing the procedure are kept as low as reasonably achievable consistent with the required diagnostic information or the intended therapeutic effects from the procedure.

In addition, with regard to the radiation protection for a medical exposure, according to Article 7 of [7], the legal entity should also ensure:
- written protocols for each standard imaging procedure;
- information and/or instructions for patients, person willingly helping the patients, pregnant women, and/or volunteers knowingly exposed to ionizing radiation for a scientific, medical and biomedical research in relation to the medical exposure and the radiation risks; and
- information and/or instructions for patients undergoing treatment with unsealed radioactive sources and the procedure of providing the information/instructions in relation to the medical exposure and the radiation risks,
which is in line with the IAEA Basic Safety Standards No. 115 [11] and the Council Directive 97/43 [14]. The Law [1] and the same regulation [7] also gives responsibility to the legal entity for ensuring the quality control of the equipment used in the medical exposure and the programme for ensuring the quality control should be described in detail in the Radiation Protection Programme.

Some specific requirements for maintaining records on the procedure undergone by an individual including the assessed dose or the activity and the type of radiopharmaceutical applied and other data needed for patients’ dose assessment as well as requirements related to the conditions to be fulfilled when applying unsealed sources in nuclear medicine, X-ray equipment in diagnostics and sealed sources in radiotherapy are set in [9].
Within the process of optimization of the radiation protection of persons that voluntarily participate in medical and bio-medical researches and radiation protection of persons that voluntarily help patients undergoing medical treatment or diagnostic or they are visiting them, article 6, paragraph 2 of [4] promotes use of dose constraints in accordance to the IAEA Basic Safety Standards No. 115 [11] and the Council Directive 96/29 [12]. The aforementioned dose constraints are given in article 16 of [4] in accordance with the IAEA Basic Safety Standards No. 115 [11].

The legal entity should demonstrate compliance with the above mentioned radiation protection requirements for medical exposure within the licensing process. A detailed description on how these requirements are met should be given in the Radiation Protection Programme in accordance with [7].

3. CONCLUSION

The legislative and regulatory framework in the field of radiation protection (for both occupational radiation protection and radiation protection for medical exposure) in the Republic of Macedonia is established, generally, in line with the international safety standards and the EU acquis. But, however, the established framework should be improved mainly through adoption of new regulations that fully transpose the EU acquis into the national legislation, in particular, the Council Directive 97/43 [14]. Namely, definition of the medical exposure given in the Law [1] does not include the exposure of individuals as part of: their occupational health surveillance; health screening programmes; and medico-legal procedures and therefore, no specific requirements regarding such exposures have been developed so far. However, procedures established by the legal entity in case of such exposures should be described in detail in the Radiation Protection Programme in accordance with [7]. In order to facilitate better implementation of the regulatory requirements for radiation protection in medical application of ionizing radiation, it is necessary to foresee preparation and adoption of guides and manuals that are intended to specifically address how some of the provisions set in the Law [1] and the regulations adopted pursuant to this Law, are to be implemented by the legal entities.

Moreover, the knowledge of the persons involved in work with ionizing radiation in the field of radiation protection and safety is recognized as an important issue. Therefore, a specific regulation has been adopted by the RSD with regard to the type of training and the training curriculum to be provided for the radiation protection officers and the occupational exposed persons. This regulation [13] establishes the system of training necessary for ensuring an appropriate knowledge in radiation protection and safety for all persons involved in work with ionizing radiation. But however, the implementation of this regulation [13] is subject to delayed implementation. Namely, this regulation [13] does not specify any institution for providing such trainings which is to be specified in the Law according to the national legal system.

In order to comply with the international standards, the following issues were also identified as needed to be addressed on the national level:

- the necessity for establishment of quality control criteria;
- the establishment of diagnostic reference levels; and
- the optimization of imaging protocols.

Therefore, with regard to the establishment of the quality control criteria, a specific regulation is under preparation by the RSD in line with the RP 91 [15] and IAEA TECDOC Series No. 1040 [16]. Other regulation under preparation by the RSD also establishes the diagnostic reference levels on the national level in line with IAEA Basic Safety Standards No. 115 [11] and RP 109 [17].

The RSD is aware of the existing gaps in the field of radiation protection in medical application of ionizing radiation. Their overcoming represents a challenge for the RSD which could be achieved through: amending and supplementing the existing Law and preparation and adoption of new regulations, guides and manuals in the field in line with the international standards and the EU acquis; enhancing the institutional cooperation; preparation and implementation of specific national projects; promotion of the safety culture as well as further strengthening the control over the ionizing radiation sources in the Republic of Macedonia.

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THERMOLUMINESCENT SIGNAL FADING OF ENCAPSULATED LiF:Mg,Ti DETECTORS IN PTFE-Teflon®

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Abstract – Fading is a process when the latent information of a detector is unintentionally lost mainly due to the thermal influence. Thermoluminescent (TL) detectors have different sensitivities as far as the fading effect. Encapsulated TL detectors mounted within shielded filter holders are used during the personal monitoring of occupationally exposed persons in R. Macedonia. PTFE-Teflon® polymer is an example of encapsulation material that has a temperature resistance and it allows the luminescence signal to pass through. Since the encapsulated TL detectors cannot be submitted to annealing treatment in an oven, another fading reduction method is needed. The TL evaluation method suggested in this work is based on a specific glow-curve region. Irradiations were conducted using ⁹⁰Sr/⁹⁰Y source. Post-irradiation fade investigations were conducted for evaluation periods that varied up to 4 months. Two areas of the TL glow-curve were selected with the WimRems software. They correspond to the high and the low fading emission peaks (the lower temperature peaks display a greater degree of thermal fading than the higher temperature peaks). Post-irradiation fade is a contributing factor that affects the response of a thermoluminescent (TL) phosphor as a function of time.

PTFE – Polytetrafluoroethylene most well known by the DuPont brand name Teflon®

Keywords – fading, thermoluminiscence, LiF, TLD, ThermoFisher

1. INTRODUCTION

Thermoluminescence is the emission of light from an insulator or semiconductor when it is heated. Thermoluminescence is the thermally stimulated emission of light following the previous absorption of energy from radiation. In this statement the three essential components necessary for the production of thermoluminescence can be found. Firstly, the material must be an insulator or semiconductor. Metals do not exhibit luminescent properties. Secondly, the material must have at some time absorbed energy during the exposure to radiation. Thirdly, the luminescence emission is triggered by heating the material. In addition, there is one important property of thermoluminescence which cannot be inferred from this statement as it stands at present. It is a particular characteristic of thermoluminescence that, once heated to excite the light emission, the material cannot be made to emit thermoluminescence again by simply cooling the specimen and reheating. The process can be triggered again only if the material is re-exposed to radiation.

Fading is the process in which there is an unintentional loss of the latent information, that is, its response. There are many causes of the process of fading, but the thermal is the main one. In the thermal fading, the traps that present lower entrapment energy will fade faster than the more energetic ones, due to their higher probability of transition. This can generate large errors in the dose assessment.

The principles of the thermal fading have essentially been dealt with in the discussion of the isothermal analysis of the thermoluminescence glow curves. The main point is that if the trap depth $E$ is too small then a severe fading of the signal will occur, both during irradiation and between irradiation and readout. For dosimetry purposes, therefore, it is desirable for the detector to be characterized by a glow curve with a peak at some temperature. This temperature range usually ensures that the trap depth is large enough ($E > kT$) so that no appreciable trap emptying takes place, but also it is low enough so that the interference from the black-body background signal is negligible. [1]

The development and implementation of a dosimetric system includes the realization of performance tests of the dosimeter that will be used. These tests assess the consistency of the obtained outcomes by determining the characteristics of the reference adopted. These patterns of development are described by IAEA’s Safety Standard RS-G-1.3 [2] and IEC 1066 [3].
2. MATERIALS AND METHODS

The equipment used for the tests included a Harshaw model 6600 PLUS Automated TLD Reader with WinREMS (Windows based Radiation Evaluation and Management System), an internal ⁹⁰Sr/⁹⁰Y beta irradiator source (Å=0.5 mCi/2006) and the detector element used in this study is crystal LiF:Mg,Ti (TLD-100), manufactured by Harshaw-Bicron. This crystal LiF:Mg,Ti is encapsulated between two layers of PTFE, generating support from the thermoluminescent detector. It was noted the appropriateness of using the polymer PTFE-Teflon® to support the detector, supports the high temperature reading (300 °C) without modification of its physical form and having a low attenuation of the luminescence emitted by the TLD-100, which includes the full wavelength 350-600 nm.

A Thermo FH 40 G-L radiometer is used to follow the background radiation in the laboratory, a mercury-in-glass thermometer Laboterm for the temperature and Fisher’s barometer for the pressure.

A TLD-100 version of LiF (LiF: Mg,Ti), manufactured by Harshaw, is made with 160 ppm Mg, added to serve as the primarily trapping centers and 4 ppm Ti to provide luminescent recombination centers at which the detrapped holes and electrons recombine after being released from the trapping centers during the readout process. LiF is a useful material in dose measurement for several reasons, including its general resistance to corrosion and wear. It is barely soluble in water and the effective atomic number of LiF (8.14) is close enough to the value for tissue (7.2) to make it almost tissue equivalent. Data for some thermophysical parameters for LiF are given in Table 1.

Table 1. Thermophysical Parameters for LiF:Mg,Ti (TLD-100)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Density</td>
<td>2.635</td>
<td>g/cm³</td>
</tr>
<tr>
<td>Heat Capacity</td>
<td>1.604</td>
<td>J/(gK)</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>0.74 x 10⁻³ (at 2.7 µm)</td>
<td>1/µm</td>
</tr>
<tr>
<td>Thermal conduction coefficient</td>
<td>1800 (at 20°C)</td>
<td>W/(m·K)</td>
</tr>
<tr>
<td>Chip thickness</td>
<td>0.89</td>
<td>mm</td>
</tr>
</tbody>
</table>

Source: Thermo Fisher Scientific

The method of thermoluminescence is a relative method and therefore the TLDs have to be calibrated against absolute dosimetry systems such as a calibrated ion chamber. A ¹³⁷Cs gamma source is used for calibration of the dosimetric system in terms of dose equivalent. Before beginning any calibration procedures, a fixed fade time is established for each of the calibration procedures. It is important that the time between irradiation and readout for all dosimeters is consistent in order to keep fading the same from one calibration to the next. The specific length of this time is not as important as its consistency. Manufacturer’s recommendations are that the fade time should be no less than thirty minutes. Otherwise, any length of time that suits operations is acceptable, but it must be consistent from one time to the next. [4]

In order to reduce the fading effect without the need of a thermal reading, a method of charge acquisition can be adopted, which is going to be related to a single region of the thermoluminescent glow curve emission. Two regions of the TL glow curve were selected through the WimRems software; they were related to the emission peak that presented a high and a low degree of fading including two regions of interest (ROI), the channels 070 to 108 (ROI-1) and the 108 to 180 (ROI-2), respectively, from a total of 200 channels in which the other ones were discarded. Region 1 (ROI-1) was identified as the “fading” region and region 2 (ROI-2) as the “dose” region, due to its agreement with the format of the emission curve found after a period of four months, as shown in Figure 1. Region 2 represents the emission peaks 3, 4 and 5 of the TLD 100, being used for the dosimetry.

So, in order to analyze the fading process 5 TL cards were used, each one with two detectors, resulting in a total of 10 measurements for each assessment. One crystal was discarded, so there were 9 measurements for each assessment. The detectors were given an absorbed dose of around 2.5 mGy from the ⁹⁰Sr/⁹⁰Y beta irradiator source. After the irradiation, the detectors were read in the selected time for the analyses of the fading effects, as shown on Table 2. The temperature was controlled only during the working hours and set at (23 ± 3) °C. During the night the temperature dropped in winter to 15°C and rose in summer to 28°C. Ambient dose equivalent rate in the storage room was (75 - 175) nSv/h.

Table 2. Fading in variation in time

<table>
<thead>
<tr>
<th>t [h]</th>
<th>Relative Intensity [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>f-fad</td>
</tr>
<tr>
<td>0</td>
<td>100.0%</td>
</tr>
<tr>
<td>0.5</td>
<td>98.7%</td>
</tr>
<tr>
<td>1</td>
<td>98.6%</td>
</tr>
<tr>
<td>2</td>
<td>95.4%</td>
</tr>
<tr>
<td>3</td>
<td>97.6%</td>
</tr>
<tr>
<td>12</td>
<td>93.3%</td>
</tr>
<tr>
<td>24</td>
<td>93.1%</td>
</tr>
<tr>
<td>48</td>
<td>91.1%</td>
</tr>
<tr>
<td>72</td>
<td>92.4%</td>
</tr>
<tr>
<td>168</td>
<td>84.7%</td>
</tr>
<tr>
<td>720</td>
<td>78.6%</td>
</tr>
<tr>
<td>1440</td>
<td>76.6%</td>
</tr>
<tr>
<td>2160</td>
<td>78.5%</td>
</tr>
<tr>
<td>2880</td>
<td>77.2%</td>
</tr>
</tbody>
</table>
3. RESULTS

By using the data from Table 2, it was possible to determine graphically the relative fading in the regions 1 and 2 (Fig2).

4. CONCLUSION

The dosimetric peak temperatures of LiF:Mg,Ti material are between 245 and 300 °C. They are known as peaks 3, 4 and 5. These are stable peaks. The low temperature peaks are the major players in the fade process.

Analysing the whole pick area, the stability of the fading signal in a period of 1 month after irradiation can be noticed. This is because the pick 2 is preserved only in few days after irradiation, which fades very fast. From the data in Table 2 fading is around 21.5% – 23.5% in a period up to 4 months. The first peak area showed around 50% of fading in about 24 hours. Through this analyses it was verified that for the LiF:Mg,Ti (TLD-100) detector encapsulated in PTFE-Teflon, for the second pick area, the fading...
overestimates 13% for a period of three days, 1.6% for a period of two months and 2.7% for a period of four months.

This reading procedure, which works specifically on some regions of the thermoluminescent emission curve, can be used to reduce the effects that the fading causes in the final reading of the dosimetric systems. This can be done either mathematically or by removing the low temperature peaks.

For further research works the mathematical function for the fading factor can be found.

5. REFERENCES


MONTE CARLO SIMULATION OF BUILDUP FACTORS FOR SINGLE AND MULTI-LAYER SHIELDS BY USING PENELOPE CODE

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Abstract – A historical overview of the development of buildup factor estimation techniques for single and multi-layer shields is presented. The buildup factors for lead, water and iron, as well as for various combinations of these materials for point isotropic source and pencil beam of photons with energies of 1 MeV and 3 MeV, for different thicknesses of the layers, are calculated by using the computer code system PENELOPE. It is shown that there is a good agreement between the values for the buildup factors for multi-layer shields obtained by Monte Carlo simulation and by using different approximation formulas. It is obtained that the values for the buildup factors by using the Blizard method can be used as rough approximations in the shielding design.

Keywords – buildup factors, point isotropic source, pencil beam of photons, Monte Carlo simulation, PENELOPE code

1. INTRODUCTION

The shielding concepts were developed during the World War II, particularly at the time of the Manhattan Project, when the term buildup factor was used for the first time. In 1947 at Oak Ridge National Laboratory the first research program in nuclear reactor shielding (X-10 graphite reactor) under the direction of Everitt Blizard was organized. The early shielding studies were penetrations and heating in concrete shields due to neutron and gamma-ray absorption, neutron attenuation, shielding material properties, the creation of capture and inelastic scattering gamma rays, reflection and streaming of neutrons and gamma rays through ducts and passages, and radiation effects on materials. The next steps were the researches on electron and photon transport in a material, developing methods for solving the transport equation describing the spatial, energy, and angular distributions of particle fluences arising from fixed sources.

In collaboration with the Bureau of Standards, Goldstein and Wilkins (1954) made use of the SEAC digital computer at the Bureau for evaluation of energy spectra and buildup factors for many materials and a broad range of photon energies. The results, known widely as NYO-3075, for many years represented the prime source of buildup factor data for use in shielding design. After that, series of scientific papers were published in which different approximation formulas and techniques for calculating the buildup factors were developed: Taylor (1954), Berger (1956), and Capo (1959).

In the 1940’s, John von Neumann and Stanislaw Ulam at Los Alamos used the Monte Carlo method for simulation of radiation transport computationally. Neutron transport calculations were performed in 1948 using the ENIAC digital computer. Many computer codes for solving the Boltzmann transport equation for neutrons and gamma rays were developed (DTF – Lathrop, 1965; DOT – Mynatt et al., 1969; ANISN – Engle, 1967), the gamma-ray “point-kernel” codes (Engle et al., 1966; Malenfant, 1967), the multi-group Monte Carlo code for neutron and gamma ray transport, MORSE (Straker et al., 1970), etc. In 1962 the Radiation Shielding Information Computational Center (RSICC) at Oak Ridge National Laboratory was established in order to provide an in-depth coverage of the radiation transport field and to meet the needs of the international shielding community.

The computations of the buildup factors continued to be made over the years. Eisenhauer and Simmons (1975) and Chilton et al. (1980) published tables of buildup factors; Simmons (1973) developed the moments method code; Morris et al. (1975) incorporated the positron annihilation in the calculations; Subbaiah et al. (1982), and Gopinath et al. (1987) used the ASFIT code; Takeuchi et al. (1981, 1984), and Tanaka and Takeuchi (1986) used the PALLAS code for calculation of the buildup...
factors; Harima (1983), and Harima et al. (1986, 1991) developed the geometric progression formula for the buildup factors computed by the PALLAS code; etc. In [1, 2] a detailed historical overview of the buildup factors estimation is presented.

All the newest codes account for not only Compton scattering and photoelectric absorption but also positron creation and annihilation, fluorescence, and bremsstrahlung. Thus, in the PENELOPE code [3], which is used in this paper, the considered interactions are: elastic scattering of electrons and positrons; inelastic collisions of electrons and positrons; bremsstrahlung emission by electrons and positrons; positron annihilation; inner-shell ionization by electron and positron impact; coherent (Rayleigh) scattering of photons; incoherent (Compton) scattering of photons; photoelectric absorption of photons; electron-positron pair production. PENELOPE simulates the emission of characteristic x-rays and Auger electrons that result from vacancies produced in K, L and M shells by photoelectric absorption and Compton scattering of photons and by electron/positron impact. The relaxation of these vacancies is followed until the K, L and M shells are filled up, i.e. until the vacancies have migrated to N and outer shells.

2. SHIELDING OF PHOTON SOURCES

The term shielding analysis can be used in a narrow sense to refer to the quantification of how a system of shields near a source of radiation affects the radiation field at some point of interest. In a more general sense shielding analysis is the study of how radiation is created, how it migrates from its source, how it interacts with matter, how it creates microscopic changes in the medium it traverses, and how these changes affect the medium [4].

Various materials can affect the amount of radiation passing through them. Shielding is an important aspect of radiation protection. It provides more reliable way than distance and time factor of limiting personnel exposure by limiting the dose rate. The amount of shielding employed will depend on the balancing of practical necessities such as cost and the benefit expected.

When photons pass through a shield, depending on the shielding material, the thickness of the shield and the photons energy, there is a certain probability of photons interaction with the shielding material. These interactions are: coherent (Rayleigh) scattering, photoelectric effect, incoherent (Compton) scattering and pair production. Some interactions, like the photonuclear effect, for the most of the cases are negligible. Any of these interactions may result in a secondary radiation which have a probability of reaching the point of interest (detector) thus increasing the dose, flux or fluence. The attenuation of photons by a shield material is characterized as occurring in “good geometry” or “poor geometry”. In good geometry (or narrow-beam geometry) attenuation, only photons with energy equal to the initial energy reach the detector. In poor geometry (or broad-beam geometry) attenuation, a significant fraction of scattered radiation will also reach the detector, which is the most common practical situation.

2.1. Shielding of good geometry photon sources

The attenuation of narrow-beam monoenergetic photons with an initial intensity \( I_0 \) by shielding materials with thickness \( r \) and density \( \rho \) is given by the exponential attenuation law [4]

\[
I(r) = I_0 \exp(-\mu r),
\]

where \( I(r) \) is the photon intensity after passing through the shielding material, and \( \mu \) is the total linear attenuation coefficient. The total linear attenuation coefficient is actually the probability of interaction per unit distance in a shielding medium, so it is a sum of the coherent, photoelectric, incoherent (Compton) and pair production coefficients. The total linear attenuation coefficient depends on the shielding material and the photons energy. Since the photoelectric effect for low energy photons is increased in high Z materials, and the pair production interactions for high energy photons are increased in high Z materials, the values of \( \mu \) generally increases as the Z of shielding medium (absorber) increases. The ratio \( \mu / \rho \) is known as the mass attenuation coefficient. It depends on the energy of the photons and the material. The mass energy-absorption coefficient \( \mu_{en} / \rho \) involves the further emission of radiation produced by the charged particles in traveling through a medium. It is the most useful form for determining a radiation exposure or dose when a flux of x-rays or gamma-rays is known or can be determined.

2.2. Shielding of poor geometry photon sources

In case of broad-beam geometry attenuation, the scattered radiation reaches the detector so the exponential law for narrow-beam geometry can not be applied. The correction for the scattered radiation is expressed in terms of buildup factor. For broad-beam geometry the following formula can be applied [4]

\[
\psi(r) = \psi_0 B \exp(-\mu r),
\]

where \( \psi_0 \) is the unattenuated primary energy fluence, \( \psi(r) \) is the total energy fluence arriving at the detector behind a medium thickness \( r \), \( \mu \) is the narrow-beam attenuation coefficient and \( B \) is the buildup factor. The buildup factor is defined as the ratio of the total value of a specified radiation quantity, such as photon fluence, photon energy fluence, exposure or dose, when radiation passes through a medium to the contribution to that value.
from radiation reaching the point without having undergone a collision [2, 4]. The buildup factor can be obtained by experiment [5], and by solution of the Boltzmann photon transport equation, since the attenuation and scattering cross sections are known with reasonable accuracy [6].

The energy spectrum of the total energy fluence $\Phi(r, E)$ at some point of interest $r$ may be divided into unscattered component $\Phi^0(r, E)$, which consists of those photons that have reached $r$ from the source without any interaction in the attenuated medium, and the scattered component $\Phi^S(r, E)$, which consists of source photons scattered once or more times, as well as secondary photons such as x-rays and annihilation gamma rays. Thus, $\Phi(r, E) = \Phi^0(r, E) + \Phi^S(r, E)$.

The buildup factor $B(r)$ is given by [4]

$$B(r) = \frac{\int \Phi(r, E)R(E)\,dE}{\Phi^0(r, E_0)R(E_0)}$$

in which the integrations are over all possible energies $E$, and where $R(E)$ is the so-called response function of the detector. In case of monoenergetic source, with energy $E_0$, i.e. $\Phi^0(r, E) = \Phi^0(r, E_0)\delta(E - E_0)$, where $\delta(E - E_0)$ is the Dirac delta, for the buildup factor one obtains [4]

$$B(r) = \frac{\int_{E_0}^{E_0} \Phi(r, E)R(E)\,dE}{\Phi^0(r, E_0)R(E_0)}.$$  

In the literature there are many different types of buildup factors whose definition depends on the source and response function. For example, there are exposure buildup factors, absorbed-dose buildup factors, dose-equivalent buildup factors, buildup factors for point isotropic source, plane normal incidence source, plane isotropic source, etc. Also, there is a difference between the buildup factors in infinite media, semi-infinite media, or in case of layer shielding material. Some of the formulas are valid only for one type of sources, some of them in special cases can be used for different types of sources, and there are some techniques for calculation of the buildup factors for one type of sources knowing the buildup factors for another type of sources. For example, Fano et al. (1959), Goldstein (1959), Spencer (1962), Trubey (1983) introduced relation for converting the buildup factors for a plane isotropic source to buildup factors for a point source. The most of the formulas and published values for the buildup factors are for point isotropic sources in infinite media, as well as for plane normal sources (plane monodirectional perpendicular incident photons).

2.3. Mathematical approximations of buildup factors

The buildup factor can be calculated by using mathematical approximations, which are developed as an equation-of-fit for the experimental data. Two approximations, Taylor (1954) and Berger (1956), are widely used in radiation shielding calculations. There are other approximation formulas of Capo (1958), Hubbel (1963), Foderado and Hall (1981), Harima (1983), Harima et al. (1986, 1991). These approximations are used for a calculation of the buildup factor for a given shielding material through which the photons pass.

In real problems, there are interactions of the incident photons with more than one attenuation media, i.e. we should consider the buildup factor when the path from the source point to the dose point is more than one shielding material. The problem of calculating the buildup factors becomes more complex because of the different effects presented in each shielding material. The most important consideration is the production of Compton scattered photons which can be quite large for low to medium energy photons in low Z materials.

In a case of more than one parallel shielding material (N materials) there is an approximation formula for the overall buildup factor, which is given by

$$B = \prod_{i=1}^{N} B_i(\mu_i r_i).$$  

One of the earliest used approximation formula in case where the thickness of the last layer is greater then the two mean free paths (mfp), $r_N > 2/\mu_N$, is that of Blizard, which is given by

$$B = B_N\left(\sum_{i=1}^{N} \mu_i r_i\right),$$  

so the overall buildup factor is equal to that of the last layer calculated for the total optical thickness. This method of calculation of the buildup factor for multi-layer parallel shields is known as Blizard method. These two formulas can be used in practice where high accuracy is not needed.

The method of Kalos [7] for two-layer shields is applicable for a plane normal source with photon energies between 0.5 MeV and 20 MeV. For $Z_1 > Z_2$ the overall buildup factor is given by

$$B = B_2\left(l_2\right) + B_1\left(l_1\right) - B_1\left(l_1 + l_2\right) - B_2\left(l_2\right)B_1\left(l_1\right).$$  

For $Z_1 < Z_2$ the overall buildup factor is given by

$$B = B_2\left(l_2\right) + B_1\left(l_1 + l_2\right) - B_2\left(l_2\right)B_1\left(l_1\right)\times$$

$$\times \left\{B_1\left(l_1\right) - 1 - e^{-\mu_1 l_1} + \frac{\mu_1}{\mu_c}\right\}\left[1 - e^{-\mu_c l_2}\right].$$
where $\mu_C / \mu$ is the ratio of the Compton scattering cross section and the total cross section. This approximation was developed for layers of lead and water, each up to three mean free paths in thickness. These formulas can be also used for point isotropic source with satisfactory accuracy [8].

Lin and Jiang [8], proposed the following formula for the buildup factor for point isotropic source in case of a multi-layer shield:

$$B \left( \sum_{i=1}^{n-1} l_i, l_n \right) = B_n \left( l_n \right) + \left[ B_n \left( \sum_{i=1}^{n-1} l_i \right) - B_n \left( l_n \right) \right] \times K \left( \sum_{i=1}^{n-1} l_i \right) C \left( l_n \right),$$  \hspace{1cm} (9)

where $B_n \left( l_n \right)$ is a buildup factor of the $n$-th layer, $l_n$ is the optical thickness of the $n$-th layer,

$$K \left( \sum_{i=1}^{n-1} l_i \right) = \frac{B \left( \sum_{i=1}^{n-1} l_i, l_{n-1} \right) - 1}{B_n \left( l_{n-1} \right) - 1},$$  \hspace{1cm} (10)

$$C \left( l_n \right) = \exp \left( -1.08 \gamma l_n \right) + 1.13 \beta L \left( l_n \right) \quad \text{for high Z material}$$

$$- \text{layer}, \quad \text{followed by a low Z material}$$

$$C \left( l_n \right) = 0.8 L \left( l_n \right) + \frac{\gamma}{K} \exp \left( -l_n \right) \quad \text{for low Z material}$$

$$\beta = \left( \frac{\mu_C}{\rho} \right)_{n-1} \left( \frac{\mu}{\rho} \right)_{n-1},$$

$$\gamma = \left( \frac{\mu_C}{\rho} \right)^{-1} \left( \frac{\mu}{\rho} \right)^{-1},$$

$L \left( l_n \right) = \frac{B_n \left( l_n \right) + 1}{B_n \left( l_{n-1} \right) + 1} \left( 1 - e^{-l_n} \right)$, $\mu_C / \rho$ is the total mass attenuation coefficient, and $\mu_C / \rho$ is the Compton mass attenuation coefficient.

### 3. PENELLOPE CODE

The PENELLOPE is a Monte Carlo algorithm and a FORTRAN 77 computer code for simulation of coupled electron-photon transport in arbitrary materials for a wide energy range, from a few hundred eV to about 1 GeV. The name is an acronym that stands for PENetration and Energy LOss of Positrons and Electrons (photon simulation was introduced later). The simulation algorithm is based on a scattering model that combines numerical databases with analytical cross section models for the different interaction mechanisms. In this work PENELLOPE 2005 version [3] is used.

In the simulation it is considered that the particle transport can be modeled as a Markov process, i.e., “future values of a random variable (interaction event) are statistically determined by present events and depend only on the event immediately preceding”. Because of the Markovian character of the transport, the generation of a particle history can be stopped at an arbitrary state (any point of the track) and the simulation from this state can be resumed without introducing any bias in the results.

PENELLOPE reads the required information about each material (which includes tables of physical properties, interaction cross sections and physical information) from the input material data file. The program includes information for a set of 280 materials, for the elements with atomic numbers from 1 to 99, and for 181 compounds and mixtures.

For making simulation with the PENELLOPE code a geometry file is needed. With the programme any material system consisting of homogeneous bodies limited by quadric surfaces can be described. The bodies of the material system can be grouped into modules (connected volumes, limited by quadric surfaces that contain one or several bodies); the modules can form larger modules, and so on.

With this programme, impact and energy-deposition detectors can be defined. The output spectrum from the impact detector is the energy distribution of the particles that entered any of the active bodies coming from a body that is not active (i.e. that is not a part of the detector). The output spectrum of an energy-deposition detector is the distribution of absorbed energy (per primary shower) in the active bodies.

### 4. SIMULATION RESULTS AND COMPARISON

In this chapter results of the simulation for exposure, dose-equivalent and absorbed-dose buildup factors for monoenergetic point isotropic source, as well as for absorbed-dose buildup factor for pencil beam of photons in single and multilayer shields are presented [9].

#### 4.1. Simulation results for point isotropic source

As it was mentioned, the buildup factors depend on the energy of the incident photons $E_0$, the shielding material and the response function of the detector. We calculate the exposure, the dose-equivalent and the absorbed dose buildup factors [10] in case where an impact detector is used.

From practical point of view in the formulas for the buildup factors instead of integration the summation is used, so for the buildup factors it is obtained:

- exposure buildup factor:

$$B_{t} = \frac{\sum_{i} f_{t} (E_i) p (E_i) E_i}{\sum_{i} f_{t} (E_0) p (E_0) E_0},$$  \hspace{1cm} (11)

where $f_t (E)$ is the energy-flux to exposure rate conversion factor [10]; $p(E_i)$ is the photon
probability of having energy \( E_i \) given in eV: particle, taken from the simulation, which reaches the detector; \( E_{\text{min}} \) is the minimum energy of the photon which reaches the detector and \( E_0 \) is the initial energy of the photons;

- dose-equivalent buildup factor:

\[
B_{\text{rem}} = \sum_{E = E_{\text{min}}}^{E_0} \frac{f_{\text{rem}}(E_i) p(E_i) E_i}{f_j(E_0) p(E_0) E_0},
\]

where \( f_{\text{rem}}(E) \) is the energy-flux to dose-equivalent conversion factor [10]; and

- absorbed dose buildup factor:

\[
B_a = \sum_{E = E_{\text{min}}}^{E_0} \frac{\mu_{\text{abs}}(E)}{\rho} \frac{p(E_i) E_i}{p(E_0) E_0},
\]

where \( \mu_{\text{abs}}(E) / \rho \) is the mass energy-absorption coefficient [6]. It is used to obtain the absorbed dose rate when the bremsstrahlung is taken into account in the transport calculations. In case of exclusion of the bremsstrahlung, instead of the mass-energy absorption coefficient, the mass-energy transfer coefficient \( \mu_i(E) / \rho \) is used, so the absorbed-dose buildup factor correspond to the medium-kerma buildup factor.

In case of a point isotropic source with initial photon energy of 3 MeV the simulations for the exposure, the dose-equivalent and the absorbed-dose buildup factors are made for lead, water and combinations of lead and water, and for different thicknesses of the layers expressed in mfp (mfp is a mean free path, which is defined as the average path length between collisions). The results which are given in the table 1 are in good agreement with those given in [8], obtained by using the Monte Carlo code EGS4. In the simulations an impact detector is used. The detector is a spherical water detector with radius 1 cm. The energy window used in the simulation is from 10 keV to 3.1 MeV, and the number of channels is 1000.

### Table 1. Buildup factors for point isotropic source

<table>
<thead>
<tr>
<th>Thickness of the layer(s)</th>
<th>( B_x )</th>
<th>( B_{\text{rem}} )</th>
<th>( B_a )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lead (1 mfp)</td>
<td>1.39</td>
<td>1.41</td>
<td>1.39</td>
</tr>
<tr>
<td>Lead (2 mfp)</td>
<td>1.70</td>
<td>1.73</td>
<td>1.70</td>
</tr>
<tr>
<td>Lead (4 mfp)</td>
<td>2.56</td>
<td>2.59</td>
<td>2.55</td>
</tr>
<tr>
<td>Water (1 mfp)</td>
<td>1.58</td>
<td>1.63</td>
<td>1.58</td>
</tr>
<tr>
<td>Water (2 mfp)</td>
<td>2.20</td>
<td>2.31</td>
<td>2.19</td>
</tr>
<tr>
<td>Lead (1 mfp) + Water (1 mfp)</td>
<td>2.00</td>
<td>2.09</td>
<td>2.00</td>
</tr>
<tr>
<td>Water (1 mfp) + Lead (1 mfp)</td>
<td>1.92</td>
<td>1.95</td>
<td>1.92</td>
</tr>
</tbody>
</table>

### 4.2. Simulation results for pencil beam of photons

In case of a pencil beam of photons we use an energy deposition detector, so we calculate the absorbed dose buildup factor:

\[
B_a = \frac{\sum_{E_0}^{E_n} p(E_i) E_i}{p(E_0) E_0}.
\]

In the simulation the initial photons energy is 1 MeV and the shielding materials are lead, iron and water and their combinations. An energy deposition germanium detector is used. For this purpose the pencil beam, the parallel layer shields and the energy deposition detector, which is limited by two parallel infinite planes, are used. The energy window used in the simulation is from 10 keV to 1.1 MeV, and the number of channels is 1000. The results can be compared with those for the plane normal source, parallel layer shields and small detector. This can be done according to the reciprocity theorem [4], which stands: If the total source strength is kept constant then the average dose in the detector from the source is the same as the average dose that would occur in the place of the source if the source strength were uniformly distributed throughout the detector. The results are given in the table 2.

### Table 2. Buildup factors for pencil beam of photons

<table>
<thead>
<tr>
<th>Thickness of the layer(s)</th>
<th>( B_x )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lead (1 mfp)</td>
<td>1.38</td>
</tr>
<tr>
<td>Lead (2 mfp)</td>
<td>1.62</td>
</tr>
<tr>
<td>Lead (3 mfp)</td>
<td>1.82</td>
</tr>
<tr>
<td>Lead (4 mfp)</td>
<td>1.97</td>
</tr>
<tr>
<td>Iron (1 mfp)</td>
<td>1.62</td>
</tr>
<tr>
<td>Iron (2 mfp)</td>
<td>2.19</td>
</tr>
<tr>
<td>Water (1 mfp)</td>
<td>1.67</td>
</tr>
<tr>
<td>Water (2 mfp)</td>
<td>2.33</td>
</tr>
<tr>
<td>Water (3 mfp)</td>
<td>3.04</td>
</tr>
<tr>
<td>Water (4 mfp)</td>
<td>3.85</td>
</tr>
<tr>
<td>Water (5 mfp)</td>
<td>4.79</td>
</tr>
<tr>
<td>Lead (1 mfp) + Water (1 mfp)</td>
<td>2.03</td>
</tr>
<tr>
<td>Water (1 mfp) + Lead (1 mfp)</td>
<td>1.75</td>
</tr>
<tr>
<td>Lead (1 mfp) + Water (2 mfp)</td>
<td>2.74</td>
</tr>
<tr>
<td>Lead (1 mfp) + Water (3 mfp)</td>
<td>3.54</td>
</tr>
<tr>
<td>Lead (2 mfp) + Water (3 mfp)</td>
<td>3.95</td>
</tr>
<tr>
<td>Lead (1 mfp) + Iron (1 mfp) + Water (1 mfp)</td>
<td>2.70</td>
</tr>
<tr>
<td>Lead (1 mfp) + Iron (1 mfp) + Water (3 mfp)</td>
<td>4.39</td>
</tr>
</tbody>
</table>

### 4.3. Comparison

The obtained buildup factors for single layer shield are slightly different in comparison to those obtained for infinite media. It is in an agreement with the results of Shultis and Faw [4], for the dependence of the buildup factor for finite media \( B_x \) on the infinite media buildup factor \( B_{\text{rem}} \). The adjustment factor is
given by \( \frac{B_x - 1}{B_x} \), for which there are tables on its dependence on the energy of the source [11].

In case of a point isotropic source the exposure buildup factors for a shield of lead (1 mfp) and water (1 mfp) are as follows: 2.00 (simulation), 1.84 (Lin and Jiang) and 2.20 (Blizard); the dose-equivalent buildup factors are: 2.09 (simulation), 1.89 (Lin and Jiang) and 2.30 (Blizard); and the absorbed-dose buildup factors are: 2.00 (simulation), 1.83 (Lin and Jiang) and 2.20 (Blizard).

In case of pencil beam of photons the absorbed-dose buildup factors are as follows: 2.03 (simulation), 2.04 (Kalos) and 2.30 (Blizard) for layer of lead (1 mfp) and water (1 mfp); 1.75 (simulation), 1.67 (Kalos) and 2.30 (Blizard) for layers of water (1 mfp) and lead (1 mfp); 3.54 (simulation), 3.50 (Kalos) and 3.85 (Blizard) for layers of lead (1 mfp) and water (3 mfp); 3.95 (simulation), 3.86 (Kalos) and 4.79 (Blizard) for layers of lead (1 mfp), iron (1 mfp) and water (1 mfp); 4.39 (simulation) and 4.79 (Blizard) for layers of lead (1 mfp), iron (1 mfp) and water (3 mfp).

5. CONCLUSION

The radiation shielding is a very important part of the radiation physics, the nuclear engineering and the reactor physics. Shielding is an important aspect of radiation protection since it can be a form of radiation control, and it provides more reliable way than distance and time factor of limiting personnel exposure by limiting the dose rate.

As it was presented, there are different types of buildup factors and it is very important to use the appropriate buildup factors and the appropriate tables for a shielding design. A special attention needs to be paid in defining the buildup factors, which quantity is used for the calculation, i.e. the response function.

The results showed that the PENELOPE code can be used for calculation of buildup factors and the Blizard method can be used as a rough approximation in the shielding design. The successful results for the buildup factors encourage using the PENELOPE code for making shielding and dose calculations for more complex geometries.

Acknowledgement: The author would like to thank to Prof. M.J. Anagnostakis from the National Technical University of Athens (NTUA) and K. Karopoulois, PhD student at the NTUA, for their help and cooperation in learning the PENELOPE code.

6. REFERENCES

Abstract – In a clinical context, EEG refers to recording the brain’s spontaneous electric activity, using small electrodes placed on the scalp. The signals collected are electric “potentials” measured between two electrodes. Usually, for a healthy adult, these signals have small voltage (10µV to 100 µV) and frequencies in the 0-40 Hz range. In the scientific literature, there are mentioned EEG signals and evoked potentials that have higher frequencies (up to 600Hz) and amplitudes lower than 500nV. For this reason, building an amplifier capable of recording EEG signals in the nV range and with frequencies up to couple of kHz is necessary to continue research beyond 600 Hz. We designed a very low noise amplifier that is able to measure/record EEG signals in the nV range over a very large frequency bandwidth (0.09 Hz -385 kHz).

Keywords – instrumentation amplifier, EEG signals, evoked potentials

1. INTRODUCTION

EEG signals have been studied since 1924, when Hans Berger recorded the first EEG signal using silver electrodes and a galvanometer. Alpha waves (8-12) Hz were the first to be discovered. Due to mechanical limitations of the pen-writer EEG recording units, used until late 1980s, the clinical diagnostics based on EEG signals are related only to the low-end frequency spectrum, up to 30 - 40 Hz. The digital EEG made possible the recording of signals within a wider frequency range. In the last couple of years, the scientific literature mentions ripples during sleep at 80-200 Hz [1] and somatosensory evoked potentials (SEPs) having 600 Hz and amplitudes <500 nV [2]. Taking these recent results into account, we decided to conceive and to build an amplifier able to record EEG signals in the nV range over a lot wider frequency range.

2. THE INSTRUMENTATION AMPLIFIER

Our amplifier is an instrumentation amplifier with differential inputs [3]. The particularities of this circuit will be discussed in the following paragraphs. A block scheme of the amplifier is presented below (Fig. 1).

Fig. 1 – Block scheme of the amplifier

The amplifier is built in a small metal box, with SMA connectors on both inputs, a BNC connector for the output and two RCA connectors for the battery recharge circuit. (Fig. 2)
2.1 First Gain Stage

For each input signal, a pair of cascades is used. The cascade consists of a JFET (2SK170) transistor and a BJT (BC550) transistor. As a result the input – output isolation is improved and the amplifier has a larger bandwidth. The input impedance is 10 MΩ per channel, 20 MΩ for a differential signal and 5 MΩ for the common mode signal. Two cascades in parallel for each input signal have a great impact on the noise level, which is lower than if only one cascade was used. As a drawback of using cascades, (having 4xJFETs and 4xBJTs used only for the input channels), is that the batteries which power the circuit must be recharged more often, as they drain faster. The static operation point of the four 2SK170 transistors are chosen in order to minimize the noise level through this gain stage. Therefore the drain current is set to $I_D = 4 mA$ (Fig. 3) and the drain-source voltage is set to $U_{DS} = 6.6 V$ (Fig. 4), which, according to the manufacturer’s data sheet [4], ensures an equivalent input noise voltage with a value smaller than $1 nV/\sqrt{Hz}$ (Fig. 5).

\[ E_{n} = I_{D} \]

\[ U_{DS} = 6.6 V \]

2.2 Operational Amplifiers

High-end LT1028A operational amplifiers (op amps) are used in the feedback loops with the input stage of the amplifier. The voltage noise density of these op amps is as low as $0.85 nV/\sqrt{Hz}$ at 1kHz and $1 nV/\sqrt{Hz}$ at 10Hz [5] (Fig. 6). Two LT1028 are used into the circuit. Both of them are powered by a differential power supply, having 16.8V on the positive side and -8.4V on the negative side.

\[ V_{DS} = \pm 15V \]

\[ T_A = 25^\circ C \]

2.3 Negative Reaction Loops

Two negative reaction loops are used in this circuit. One is used to realize an instrumentation amplifier. The output impedance of the amplifier is 50 Ω. The second loop is used to maintain a certain drain current value through the 2SK170 transistors.
2.4 Overload Protection
The amplifier is designed with overload protection against output signals with amplitudes higher than +/- 1.2V. Two LEDs indicate whether the amplifier is overloaded on the positive or the negative side.

2.5 Battery Recharge Circuit
Using rechargeable batteries to power the amplifier is a great solution to avoid power line noise. Therefore, a small battery recharge circuit is added to the amplifier. A two-position switch can change between measuring mode and battery recharge mode. Both modes are totally independent of each other.

3. MEASUREMENTS AND RESULTS

3.1 Overall characteristics
Differential voltage gain: 36 dB
Gain bandwidth: 0.09 Hz - 385 kHz
Common mode rejection ratio: 95 dB
Differential input resistance: 20 MΩ
Output resistance: 50 Ω
Equivalent input noise voltage: $7\,nV/\sqrt{Hz}$

3.2 Gain and Bandwidth
The differential gain of the amplifier is 36 dB within 0.09 Hz - 385 kHz frequency range. (Fig. 7)

3.3 Noise Measurements Using Lock-In Amplifier
The internal noise of the amplifier has been measured using a Stanford Research SR530 Lock-In Amplifier. The 1/f corner is at 22Hz. The equivalent input noise voltage is $7nV/\sqrt{Hz}$ frequencies higher than 22 Hz (Fig. 8).

3.4 Common mode rejection ratio
The common mode rejection ratio is one of the most important parameters of an instrumentation amplifier. During an EEG recording, where the signal is apparently random for a defined point on the scalp, but definitely different than any other signal recorded at a small distance around that point, it is important to reject signal components that are the same on both input channels. A common mode rejection ratio of 95dB has been reached (Fig. 9).

4. CONCLUSION
Looking at the characteristics of this amplifier, we can conclude that it is suitable for EEG signal recordings and evoked potentials too. With an input noise signal of $7nV/\sqrt{Hz}$, the amplifier is able to measure very small signals (in the nV range), which have frequencies in the 0.09 Hz – 385 kHz range. Also, the small dimensions, light weight and the battery power supply make the amplifier suitable for a wider range of applications (as emergency units, high school labs, etc).
5. REFERENCES


[5] Linear Technology LT1028/LT1128 Datasheet
FTIR-MICROSPECTROSCOPY AS A DIAGNOSTIC METHOD FOR CANCER CELLS

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Abstract – In the present study we have compared the spectral behavior of malignant cells with normal untransformed cells using microscopic Fourier-Transform Infrared (FTIR-M) spectroscopy in order to evaluate the potential of this technique for early detection of cancer cells. Cells were transformed by infection with murine sarcoma virus (MuSV) and examined at various times post infection (p. i) by FTIR-M.

Our results showed significant and consistent differences between the normal cells and malignant cells. A considerable decrease in carbohydrates and phosphates levels was seen in malignant cells compared to the normal cells. In addition, the peak attributed to the PO2\textsuperscript{-} symmetric stretching mode at 1082 cm\textsuperscript{-1} in normal cells was shifted significantly to 1087 cm\textsuperscript{-1} in malignant cells. These spectral changes in addition to others were seen already about 24h p.i., while no morphological changes were observed at this time by optical microscope.

These results in addition to further differences in the shapes of various bands may indicate for promising potential of FTIR microscopy technique for detection of malignant cells at early stages of malignant transformation.

Keywords – FTIR microscopy, cancer cells, MuSV, primary cells

1. INTRODUCTION

In many cases the diagnosis of early malignancies of the cells/tissues is made by morphological identification and recognition. Thus, the detection of malignancy relies heavily on the clinical experience of the examiner at recognizing suspicious lesions during physical examination. Moreover, distinguishing premalignant and early malignant lesions from the more common benign inflammatory conditions can be extremely difficult even for experienced practitioners. For example cervical Pap smear cytology has an estimated 20%-40% false negative rate attributed to a combination of inadequate specimen collection, problems inherent in sampling small or inaccessible lesions, and errors in the microscopic reading of the cytology specimen [1].

For the statistics, about third of the population now living in the US will develop some type of cancer. However, early diagnosis and treatment increase the chances of survival and full recovery [2, 3].

Therefore, the development of a reagent free method for the rapid and accurate diagnosis of malignant lesions in real time would have a great potential for improving the early detection of neoplastic changes in the cells/tissues.

FTIR spectroscopy has been widely applied in biology and medicine. FTIR has expanded our knowledge on the structure, conformation and dynamics of various molecular components of the cell [4]. With the introduction of microscopy in the modern FTIR instrumentation, FTIR analysis of cells and tissues has become a reality. In recent years, there is bubbling interest to apply FTIR as a tool for the diagnosis of cancer [5-9].

In the present study we examined spectral changes due to malignant transformation of cells obtained from various origins. Our results showed significant and consistent differences between normal and malignant cells regardless to their origin at very early stages of the malignant transformation.
2. MATERIALS AND METHODS

Cells and viruses

Mouse primary fibroblast (MF) cells were obtained from the bone marrow of newborn mice. NIH/3T3 cells, a mouse fibroblast cell line, were obtained from the American Type Culture Collection (ATCC), Rockville, MD, USA.

Malignant cells (MFT) were obtained by infection of MF cells with MuSV.

Cells were grown in Dulbecco’s modified Eagle’s medium (DMEM) containing 10% fetal calf serum (FCS), 1% glutamine, 50 U/ml penicillin, 50µg/ml streptomycin and incubated at 37 °C in a humidified air containing 5% CO₂.

Clone 124 of TB cells chronically releasing Moloney MuSV-124 [10] was used to prepare the appropriate virus stock.

Cell proliferation

Cells, seeded at a concentration of 2x10⁵ cells per well in 24 well plate, were incubated for five days at 37°C in RPMI medium supplemented with 10% newborn calf serum (NBCS) and the antibiotics penicillin, streptomycin and neomycin. Each day, the cells were examined for morphological changes, and the number of cells was counted with a hemocytometer.

Cell infection and determination of cell transformation

A monolayer of cells grown in 24 well tissue culture plate was treated with 8 µg/ml of polybrene (a cationic polymer required for neutralizing the negative charge of the cell membrane) for 24 h before infection with the virus. Excess polybrene was then removed, and the cells were incubated at 37°C for 2 h with the infecting virus (MuSV-124) at various concentrations in RPMI medium containing 2% of NBCS. The unabsorbed virus particles were removed, fresh medium containing 2% NBCS was added, and the monolayers were incubated at 37°C. After 2-3 days, the cell cultures were examined for the appearance of malignant transformed cells.

Soft agar assay

A mixture of 25% of 2% Bacto agar, 25% of RPMI × 2 (concentrated medium), 20% of NBCS and 30% of RPMI was prepared, and 4 ml of this mixture was poured into a number of 50-mm petri dishes. The mixture was left to polymerize at room temperature for about 30 min. This procedure gave a solid agar (0.5%) layer. On each solid layer was poured 1 ml of 0.36% agar containing the test cells. This upper layer was prepared by mixing of 18% of 2% Bacto agar, 18% of RPMI × 2, 20% of NBCS and 44% of RPMI. About 10⁴ cells were added to each plate. The plates were left at room temperature for about 20 min and then incubated at 37°C in humidified air containing 5% CO₂ for about 14 days. At the end of the incubation period, colonies of transformed cells were counted under a light microscope.

Preparation of slides

Since ordinary glass slides exhibit strong absorption in the wavelength range of interest to us, we used zinc selenide crystals, which are highly transparent to IR radiation. Normal cells from passage 3-5 or transformed cells (from a fully transformed cell culture) were washed twice with saline and picked up from the tissue culture plates after treatment with trypsin (0.25%) for 1 min. The cells were pelleted by centrifugation at 1000 rpm for 5 min. Each pellet was washed twice with saline and resuspended in 100 µl of saline. The number of cells was counted with a hemocytometer, and all tested samples were pelleted again and resuspended in an appropriate volume of saline to give a concentration of 1000 cells/µl. A drop of 1 µl of each sample was placed on a certain area on the selenide crystal, air dried for 4h. and examined by FTIR microscopy. The radius of such 1µl drop was about 1 mm.

FTIR spectra

FTIR measurements were performed in transmission mode with a liquid nitrogen-cooled MCT detector of FTIR microscope (Bruker IRScope II) coupled to the FTIR spectrometer (BRUKER EQUINOX model 55/S, OPUS software). The spectra were obtained in the wave number range of 600-4000 cm⁻¹ in the mid-IR region. A spectrum was taken as an average of 128 scans to increase the signal to noise ratio, and the spectral resolution was at 4 cm⁻¹. The aperture used in this study was 100 microns, since we found that this aperture gives best ratio signal/noise. At lower apertures the quality of spectra was bad due to high levels of noise. In addition, at apertures lower than 20 µm, there is a diffraction of IR light. Baseline correction and normalization were performed for all the spectra by OPUS software. Baseline correction was done by rubber band method. For the construction of the baseline the spectrum is divided up in n ranges of equal size. In each range the minimum y-value is determined. The baseline is created by connecting of minima with straight lines. Starting from “below” a rubber band is stretched over this curve. The rubber band is the baseline. The baseline points that don’t lie on the rubber band are discarded.

Normalization was done by vector method. The average y-value of the spectrum is calculated first. This average value is then subtracted from the spectrum so that the middle of the spectrum is pulled down to y = 0. The sum of the squares of all y-values is then calculated and the spectrum is divided by the square root of this sum. The vector norm of result spectrum is 1. Peak positions were determined using standard method by OPUS software. For each cell type, the spectrum was taken as the average of five different measurements at various sites of the sample.
Each experiment with each cell type was repeated five times.

It is important to mention that there are no considerable differences in spectra from various sites; standard deviation (SD) didn’t exceed 0.005.

3. RESULTS

Cell characteristics

In the present study various primary cells (1-2 passages in culture), cell lines (thousands of passages in culture) and malignant cells transformed by retroviruses (MuSV) were used.

The primary cells differ completely in most of their characteristics and behaviour from malignant cells. Cell lines differ largely in some of their characteristics from primary cells but also differ from malignant cells. Cell lines are very stable in culture compared to primary cells which most of them are dying after several passages (about 20 passages). Primary cells replicate very slowly in culture and could not survive high densities: most of them are died after about 10 passages. However up to passages 7-8, the amount of dead cells in these cultures was negligible and did not exceed the normal death rate for cell-line cultures. In contrast, the cell lines replicate rapidly similar to malignant cells, can reach also much higher densities in cell culture compared to primary cells but they cannot reach that density of malignant cells and cannot produce foci in cell culture, they also cannot grow in soft agar. When $5 \times 10^6$ cells were injected subcutaneously to newborn mice, only malignant cells were able to produce tumors 2 weeks after injection (data not shown).

Primary cells and cell lines are not able to replicate and produce tumors in new born mice.

IR spectra of the tested cells

The spectral absorption of various normal cells and malignant cells was examined by FTIR microscopy. Our results showed significant and remarkable differences between normal and malignant cells. In general, at the differences between the various normal and malignant cells were evident in gradual increase in the intensities of the absorbance mainly at the phosphate region at 1200-1400 cm\(^{-1}\), where the malignant cells are the lowest and the primary cells are the highest (not shown results). The intensities of absorbance of the cell lines were higher than the malignant cells but lower than primary cells in both tested systems, the human and the mouse. The intensity differences for primary cells, cell lines and malignant cells for amide II were not significant in all tested cases, whereas, significantly higher intensities for amide I were obtained in malignant cells compared to primary cells and cell lines, although the discrepancy between malignant cells and cell lines was significantly smaller compared to the primary cells. It was reported that the ratio of amide I/II bands could shed light on the change in the DNA content [10]. According to this finding, our results indicate that transformed cells and cell lines had higher DNA absorption and probably, as expected, higher amount of DNA than the primary cells.

The spectra in the region 1200-1400 cm\(^{-1}\) represent PO\(_2^\neg\) asymmetric stretching vibrations [2, 11]. Our results showed a significant reduction in the intensity of the absorbance due to these PO\(_2^\neg\) vibrations for malignant cells compared to normal cells (Fig. 1A, B).

In cell lines, as expected, this intensity of absorbance was higher than malignant cells but significantly lower than primary cells.

These results are in agreement with previously documented FTIR comparisons of cancerous and normal tissues and cells [2, 11, 12].

In addition, our results show a significant and detectable shift of the peak at 1082-1083 cm\(^{-1}\) (which represent PO\(_2^\neg\) symmetric stretching band) for the normal primary cell to 1084 cm\(^{-1}\) in cell lines and 1086-1087 cm\(^{-1}\) in malignant cells regardless to their origin (Fig. 2).
Fig. 2 – FTIR microspectroscopy at the region 1050 - 1100 cm⁻¹ for the above tested cell

Fig. 3 – FTIR microspectroscopy in the region 2820-3000 cm⁻¹ at different period of times p.i. of MEF (A) and NIH/3T3 cells (B)

Fig. 3 shows the expanded spectra of both mouse primary and cell line cultures in the region 2820-3000 cm⁻¹. This figure clearly demonstrates the gradual spectral variations following cell infection. Dramatic changes are observable in case of MEF transformation compared to the moderate changes obtained in the cell line. In addition, the first morphological changes confirmed by microscopical observations and growth on soft agar (not shown results) appear considerably later than the first spectral signs. In the case of MEF primary cells, the spectral changes induced by cell transformation were much more significant compared to those induced in the NIH/3T3 transformation (Fig. 3 B). Also in MEF primary cells the first spectral signs appeared significantly earlier than the morphological changes.

4. CONCLUSION

1. The spectral differences between normal and retrovirus-transformed cells have been found as general to both kinds of tested cells and are not limited to a particular species.

2. Spectral changes due to malignant transformation can be detected at very early stages of the transformation.

3. Thus, the potential of FTIR microscopy as an advanced method for the diagnosis and probably study of malignant cells transformed by a retrovirus seems promising.

4. It is therefore worthwhile to continue with the development of FTIR microscopy for the diagnosis of malignancy.

5. REFERENCES


REGIONAL NEUROAXONAL INJURY DETECTED BY $^{1}$H 3 TESLA SPECTROSCOPIC IMAGING IN LATE ONSET TAY SACHS

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Abstract – Late-onset Tay Sachs (LOTS) is a rare lysosomal storage disorder resulting from mutations of the subunit of the lysosomal enzyme $\beta$-hexosaminidase A, which catalyzes the degradation of GM2 ganglioside. We have applied the fast encoding spectroscopic imaging technique to LOTS patients to further investigate the neurodegenerative consequences of this disease.

Keywords – spiral chemical shift imaging, late-onset Tay Sachs (LOTS), fast spectroscopic imaging.

1. INTRODUCTION

MRI is a great tool not only because it enables informative structural imaging, but also due to the fact that it offers possibilities for monitoring biochemistry in vivo. Magnetic Resonance Spectroscopic Imaging (MRSI), also known as chemical shift imaging (CSI), is an imaging technique where one obtains a spectrum of signals, e.g. brain metabolites in vivo, from an isolated volume of tissue. MRSI is based on the MR phenomenon of chemical shift, a subtle frequency shift in the signal that is dependent on the chemical environment of the particular compound. It is due to this frequency shift that there is a potential for physiological evaluation and material characterization of a volume of interest.

Chemical shift is defined as a small displacement of the resonance frequency due to shielding created by the orbital motion of the surrounding electrons in response to the main $B_0$ field. By placing a sample of biological tissue in a uniform magnet, exciting it, recording its free induction decay (FID), and then Fourier transforming the FID, the resultant MR spectrum shows resonances at different frequencies corresponding to different chemical shifts. The amount of displacement and the amplitude of the peaks in the spectrum depend on the molecular structure of the compound of interest. Being in a presence of $B_0$, the effective field experienced by the nucleus is $B_{\text{eff}} = B_0 - B_0\sigma$. Further, bearing in mind that $\omega$ is proportional to $B_0$ (the Larmor relationship), we have that

$$\omega_{\text{eff}} = \omega_0 - \omega_0\sigma = \omega_0(1 - \sigma)$$

where $\sigma$ equals the shielding constant that depends on the chemical environment, and therefore $\omega_0\sigma$ is the displacement of the resonance frequency. From this, it can be concluded that the change in frequency is proportional to the strength of the main magnetic field $B_0$.

The frequency axis in MRSI, for historical reasons, is such that the frequency decreases from left to right and it’s given in units of “parts per million” or p.p.m. The chemical shift is defined with respect to a reference frequency $\omega_0$. If the resonance frequency of the sample of interest is $\omega_s$, the chemical shift $\delta$, in p.p.m units (using (1)) is:

$$\delta = \frac{\omega_0 - \omega_s}{\omega_0} \cdot 10^6 = \frac{\omega_0(1 - \sigma_s)}{\omega_0(1 - \sigma_s)} \cdot 10^6 = \frac{\sigma_s - \sigma_s}{1 - \sigma} \cdot 10^6 \approx (\sigma_s - \sigma) \cdot 10^6$$

where the last approximation is due to the fact that $\sigma_s \ll 1$.

Fig. 1 – $^1$H MR spectrum of acetic acid (CH$_3$COOH) showing the effects of the chemical shift phenomenon. The COOH group experiences different effective $B_0$ magnetic field compared to the CH$_3$ group.
A schematic $^1$H spectrum is given in Figure 1. Due to the fact that the valency of the oxygen in the COOH group leads to an attraction of the electron away from the proton, there is less shielding for the proton in the COOH group compared to the proton in the CH$_3$ group. This is why COOH deviates more from the reference frequency (positioned at 0 p.p.m), compared to CH$_3$.

In this article we present $^1$H spectra of the human head using time-efficient sampling schemes using spiral-shaped k-space trajectories. However, it is worth mentioning that $^{13}$C and $^{31}$P CSI is of significant importance. For example, $^{31}$P spectra are used for obtaining quantitative information about chemical compounds like adenosine triphosphate (ATP), phosphocreatine (PCr), and inorganic phosphate (Pi). However, $^{13}$C and $^{31}$P spectra have significantly lower signal-to-noise ratio (SNR) compared to $^1$H spectra and therefore are more difficult to detect and quantify. This is mainly because of lower abundance and sensitivity for these nuclei.

1.1. Late-onset Tay Sachs (LOTS) disorder

Late-onset Tay Sachs (LOTS) is a rare lysosomal storage disorder resulting from mutations of the subunit of the lysosomal enzyme β-hexosaminidase A, which catalyzes the degradation of GM2 ganglioside [1]. On postmortem examination, gangliosides are found not only in cerebellar neurons but throughout deep cerebral nuclei. The main purpose of this article is to investigate these preliminary postmortem examination using magnetic resonance spectroscopic imaging, by performing in vivo regional analysis of both infra- and supratentorial brain metabolites at 3 Tesla.

2. TIME-EFFICIENT SPECTROSCOPIC IMAGING

2.1. Challenges in MRSI

The main constraint in MRSI comes from the fact that the signals of the metabolites that we are interested in are orders of magnitude lower compared to the signals coming from the water and the lipids. The concentration of the water molecules is roughly 55 M, and those of the major metabolites of interest are less than 10 mM [2]. This fact is the main reason why MRSI scans have intrinsically low SNR compared to conventional MRI of water. Figure 2 shows that compared to subcutaneous fat signals near the brain, the metabolite spectra are much lower and present a large dynamic range between the desired metabolites and the artifact signals from fat.

Furthermore, main field inhomogeneities may additionally lower the SNR in MRSI and complicate signal detection and quantification. Any undesirable variations in the main magnetic field $B_0$ will cause a shift along the frequency axis, causing overlap of the metabolites’ peaks and creating ambiguity in metabolites’ identification. These main field inhomogeneities are mainly due to susceptibility effects within the body near the boundaries of air and tissue, and thus vary from one subject to another.

2.2. Conventional CSI

A straightforward way of doing spectroscopic imaging is to do the following (in order, and per repetition time, TR) [3-4]: excite the volume of interest, “travel” to a certain $(k_x, k_y, k_z)$ position by applying short gradient lobes of appropriate area and “stop”, turn the Analog to Digital Converter (ADC) on, and finally, record the free induction decay signal (FID). This is to be repeated for all $(k_x, k_y, k_z)$ locations of interest. The number of repetition times will depend on the Field of View (FOV) and the spatial resolution requirements. This is pictorial depicted in Figure 3.

A typical single voxel spectrum is given in Figure 4. In this figure it is clear that the water and lipid signals have been significantly suppressed. In order to suppress the water signal, spectrally selective RF pulses [5] (a spin-echo pair) are used in this particular sequence design. These pulses act like band-pass filter along the $k_y$ axis: the frequency of the water signal is in their stop band, but the frequencies of the lipid signal are in their pass band mainly because at
field strengths lower than 3T, the lipid signals and the metabolites signals are spectrally close.

As mentioned, MRSI suffers from intrinsically low SNR. Since SNR in MRI is proportional to the acquisition time and the voxel size [6-7], i.e. SNR = \( V_{\text{size}} \times \frac{1}{\sqrt{4\Delta t}} \), in order to improve SNR, one could increase the voxel volume, or acquisition time, or both. Moreover, voxel size depends on the spatial resolution (lower spatial resolution gives larger voxel size), and further, the number of \((k_x, k_y, k_z)\) encodes depends on the FOV and spatial resolution parameter. Having said this, it can be concluded that FOV, spatial resolution and imaging time are not independent parameters in conventional MRSI. This is the main reason for one of the biggest disadvantages in conventional MRSI – the inflexible coupling between scan time and resolution parameters. As an example, a volumetric scan that encodes a volume at a modest 16\(^3\) k-space locations with \(\text{TR}=2s\) takes about 2 hours and 20 minutes, a prohibitive scan time for in vivo exams.

2.3. Spiral chemical shift imaging

In conventional CSI, spectral bandwidth is said to be “free” since the ADC design on the current MRI systems allows temporal sampling of as low as 0.1\(\mu s\), corresponding to very wide spectral bandwidth of 10MHz. However, on 1.5 Tesla systems, the metabolites of interests span frequencies that are within a spectral range of 400Hz. This implies that 400Hz, corresponding to temporal sampling of 2.5ms, is a sufficient spectral bandwidth for the purposes of MRSI – temporal sampling at less than 2.5ms per point is not logical since it does not provide any more information about the proton metabolites of interest.

These facts open the doors for the development of a CSI algorithm that is more efficient than the phase encoded CSI scheme. Furthermore, the hardware of the gradients has undergone major improvements in recent years, allowing possibilities for very fast k-space traversing. Nevertheless, the conventional CSI takes absolutely no advantage of the gradients’ potential, suggesting that efficient k-space sampling with time-varying gradients could be a method to overcome the rigid constraints on minimum acquisition time in phase-encoded CSI. In addition as noted in [6-7], it can be seen that the SNR does not depend on the number of voxels. This fact, combined with the ability for fast k-space sampling, provides the basis for the development of fast CSI algorithms using time-varying gradients.

Originally introduced by Adalsteinsson et al. [8], spiral CSI is a fast spectroscopic imaging algorithm that offers two orders of magnitude decrease in acquisition times compared to the conventional PE CSI. This encoding scheme samples the \((k_x, k_y, k_z)\) space simultaneously within one TR, by repeatedly playing spiral trajectories along the \(x\) and \(y\) gradients in a rather long readout period (300ms-400ms), as shown in Figure 5. For volumetric acquisitions, phase encoding is performed along the \(k_z\) axis. Given a small spatial FOV and/or low spatial resolution, it is possible to design a spiral trajectory that has a length less than, or equal to the temporal sampling rate \(\tau_s\), needed to satisfy the spectral bandwidth constraints (as noted previously, for 1.5T systems, this is 2.5ms, corresponding to 400Hz of spectral BW). This means that, for the given special case, one is able to obtain single slice spectroscopy data in only one TR!

![Fig. 5 – Simultaneous encoding along \(k_z\) axes. Every \((k_x,k_y)\) point is separated by \(\tau_s\) along the \(k_z\) axis. For volumetric acquisitions, phase encoding along \(k_z\) is performed.](image)

However, for more realistic spatial resolution and FOV parameters it is almost always impossible to traverse certain k-space volume in time \(\tau_s\). Furthermore, the value of \(\tau_s\) is inversely proportional to the field strengths (higher field strengths give wider spectral bandwidth constraints). That means that within one TR only gaps of the desired k-space are acquired, and the rest of the “unfilled” k-space data is obtained in subsequent TRs. In other words, the desired k-space spiral trajectory is divided, or decomposed into spiral trajectories (angular interleaves) that are sparser than the original, and are not longer than \(\tau_s\). The concept of interleaving is shown in Figure 6, for the case for \(N_A = 4\) angular interleaves, meaning that for this particular k-space trajectory (i.e. spatial FOV and resolution), the spiral CSI scan would last four repetition periods.

Spiral CSI trades off spatial in-plane field of view (FOV\(_{xy}\)) with spectral bandwidth. This means that for a fixed spatial FOV and spatial resolution, going to higher field means inherent increase in scan time. However, even when comparing the imaging times for ultra high field (e.g. 7T) spectroscopic imaging, the spiral CSI still provides orders of magnitude the two orders increase in time efficiency compared to PE CSI. Table 1 compares the acquisition times.
between spiral and PE CSI for two specific imaging parameters, where the time efficiency is evident.

![Diagram](image-url)

**Fig. 6 – Angular (0°, 90°, 180°, 270°) interleaves (Nₙ = 4). The final k-space trajectory is four times as dense as each individual interleaf.**

**Table 1. Comparison between the acquisition times of spiral and PE CSI for two different sets of imaging parameters**

<table>
<thead>
<tr>
<th></th>
<th>(x,y): (32x32);</th>
<th>(x,y,z): (32x32x32);</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional CSI</td>
<td>34.13 min</td>
<td>1092.27 min (~18.2h)</td>
</tr>
<tr>
<td>Spiral CSI</td>
<td>0.267 min</td>
<td>5.8 min</td>
</tr>
<tr>
<td>Conv./Spiral CSI</td>
<td>~128</td>
<td>~188</td>
</tr>
</tbody>
</table>

Having inherently low SNR, spectroscopic imaging takes great advantage of receive arrays with large number of coil elements as they provide significant SNR improvement. 32-channel receive arrays are becoming a standard, and 64-, 96- and even 128-channel arrays are in development. The major challenge when reconstructing spiral CSI data is the immense amount of data, particularly when using large number of coils. Therefore, the time efficiency provided by the spiral CSI comes at a cost of high-capacity receiver pipeline, and non-trivial trajectory designs and reconstruction algorithms. Since the spirally acquired data is non-uniformly sampled, the gridding algorithm [9] is usually used to resample the data points on a rectangular grid which can than be easily fast-Fourier-transformed. The gridding procedure is nothing more than an interpolation (or convolution) of the spiral samples with a specified kernel (e.g. Kaiser-bessel window). This process can be time consuming, since it has to be done for the spiral data at every sample point along the kₜ (or the time) axis and for every coil element used.

3. METHODS AND RESULTS

We performed single voxel MRS and 3 dimensional fast chemical shift imaging (CSI) using spiral trajectories [8] in 4 patients with LOTS (3 men and 1 woman; mean age 41 years; age range, 38-45 years) and a healthy age matched control on a MAGNETOM 3 T Tim Trio scanner (Siemens HealthCare, Erlangen, Germany). The single voxel spectroscopy acquisitions used isotropic single voxels of size 8cc placed over the basal ganglia and the cerebellum (128 averages, TR = 1.6s, TE = 35ms). Ratios of metabolites over Creatine (Cr) were calculated for N-acetysaspartate (NAA), Choline (Cho), Myoinositol (MI) and the sum of Glutamate and Glutamine (Glu + Gln).

The 3D CSI acquisitions used constant density spiral trajectories appended to a standard Siemens PRESS excitation placed wholly within the brain over 5cm thick slice-selective slab. With FOVₓᵧ = 24cm, FOVₜ = 12cm and encoding matrix of (x,y,z) = (32,32,16), the overall isotropic voxel size was 0.42cc. The spectral bandwidth was 1.6KHz, encoded over 512 samples along the frequency axis.

All 4 LOTS patients had evidence of cerebellar atrophy on conventional MRI. Single voxel MRS showed more severely perturbed metabolism in the cerebellum than in the basal ganglia. In the cerebellum NAA/Cr ratios were decreased by 54% (range 3-69%) and MI/Cr ratios were increased by 103% (range 88-124%) (Figure 7). In the basal ganglia metabolite ratios of NAA/Cr showed no difference but MI/Cr ratios were increased by an average of 66% (range 50-83%) compared to control. No consistent deviations were found in other metabolite ratios. Overall NAA/Cr ratios were lower in the cerebellum compared to the basal ganglia but the difference was greater in LOTS patients (60% versus 30% in control subject). Spatially, these findings were also confirmed when comparing three slices of the volumetric spinal CSI of the healthy volunteer and the LOTS patients. While the NAA amount seemed to be in the normal limits for the healthy volunteers (Figure 8), that was not the case for the patient data. As seen in Figure 9, the amount of NAA is significantly decreased, particularly in the slice near the ventricles.

![Image](image-url)

**Fig. 7 – Single voxel spectroscopy acquisition within the cerebellum of one LOTS patient, showing decrease in NAA/Cr, and increase in MI/Cr ratio.**
Fig. 8 – Magnitude spectra from three different slices and regions acquired in 13.5 minute long spiral CSI scan with isotropic voxel size of 0.42cc using 32-channel coil array on a healthy subject.

Fig. 8 – Multi voxel spectra from three different slices (8th, 10th, 11th) of the 3D spiral CSI acquisition of a LOTS patient. The fast encoding scheme of the spiral CSI enables one to quantify metabolites amounts in different spatial locations.
4. CONCLUSION

We have developed and implemented the spiral CSI algorithm with online gridding reconstruction [9] on Siemens scanners, and were therefore able to acquire reliable in vivo spectroscopic data. Receive arrays with large number of coil elements offer excellent benefits for volumetric, time-efficient spiral CSI. The results shown in this work illustrate that 3D volumetric CSI with 0.42-cc voxels in less then 15 minutes yield good spectral quality and SNR. Furthermore, in LOTS patients, cerebellar atrophy coincided with decreases in NAA/Cr and increases in MI/Cr, markers of neuroaxonal injury and gliosis respectively. Three-dimensional CSI may be a sensitive technique to survey various brain regions and quantify neuroaxonal injury. This works sets up the basis for usage of chemical shift imaging as a diagnostic tool for many neurodegenerative diseases by providing metabolite quantification at high spatial resolution, and therefore the spiral CSI can provide critical contribute towards providing important information about metabolite quantities in hard-to-get brain regions, like cortical areas near the skull and/or the spinal cord.

5. REFERENCES

EVALUATION OF THE INFLUENCE OF UV/IR RADIATION ON IRON RELEASE FROM FERRITIN

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Abstract – In the present work the influence of UV/IR radiation on the iron-releasing process from ferritin is investigated. The ferritins are a family of iron-storing proteins playing a key role in the biochemical reactions between iron and oxygen—processes of exclusive importance for the existence of all living organisms. The iron is stored within the ferritin core in the form of insoluble crystals containing Fe(III). Therefore for its release, the mineral matrix has to be decomposed, usually through a reduction of Fe(III) to Fe(II). Our study considers the action of UV/IR radiation on the structure of the protein molecule. Eventual changes in the ferritin conformation under the irradiation could result in the change of channel forming regions responsible for the iron efflux. This can be assess by the quantity of Fe (II) obtained in a subsequent mobilization procedure evoked by exogenous reducing agents. In our case the content of the reduced iron is determined electrochemically by the method of potentiometric titration. As already was shown, this method promises to become highly useful for quantitative evaluation of released Fe²⁺.

Keywords – ferritin, UV/IR radiation, potentiometric titration

1. INTRODUCTION

Human body is frequently exposed to infrared (IR) and ultraviolet (UV) radiation from natural and artificial sources. Normally, the first targets are skin and eyes. Conceivably, the major efforts, thus far, have been focused predominantly on research of the biological response in the corresponding tissues. [1-3]. Nevertheless, the importance of the related basic molecular processes and details in protective mechanisms on common subcellular level is usually neglected. In addition to the changes in the regulation of gene expression [4-6], two other starting points for investigation in this direction are the peroxidative reactions and closely connected with them iron intracellular redox conversions [7-10].

The role of cellular iron as a promoter for generating of reactive oxygen species (ROS) is firmly established [11-14]. Thus, iron-sequestering processes in mammalian cells are of a great importance for an effective protection against oxidative stress. The ferritin system is thought to be the main regulating machinery, keeping the proper levels of “free” iron within the cell by a precisely controlled uptake and efflux of iron atoms in and from the protein molecule [15-17]. The ferritins are family of highly conserved nanocage proteins found in all living organisms with excluding yeasts. A unique ability to accommodate huge amount of iron atoms (up to 4500) inside the shell makes them extremely suitable for the above-mentioned sequestering function. Despite the intensive research during the past decades, however, the problems around ferritin iron entry and exit (especially), are not yet fully resolved [18].

The increase of ferritin synthesis under oxidative stress is well documented [19,20]. Unfortunately, the experimental findings regarding its specific action in these conditions are ambiguous. On the one hand, some data unequivocally demonstrate the protective antioxidant function of over-expressed ferritin against toxicity of accumulated iron [21-23]. On the other hand, however, there are results suggesting just the opposite effect. There are some indications that in certain cases the excess ferritin can behave as a pro-oxidant, mainly due to the reduction of its mineral core [24-26]. Such reduction might be evoked as a result of chemical treatment, or by illumination with visible light [27], or UV-A treatment [28]. In this regard, it is a priori clear, that data obtained with chemically induced oxidative stresses cannot merely be extrapolated to those produced by irradiation. Actually, recent investigations confirm the difference...
in ferritin action during the chemically and photochemically (e.g. UV-A) provoked stresses [29].

The above considerations definitely depicted the need in further examinations of the photoinduced reduction including ferritin. In this respect, we made an attempt to assess \textit{in vitro} the mobilization of iron from ferritin under the influence of UV/IR radiation. According to previously developed experimental technique [30], potentiometric redox titration was used in the present study for quantitative evaluation of iron efflux from the protein.

2. MATERIALS AND METHODS

2.1. Reagents

Potassium chloride (KCl, Merck, Germany), at concentration of 0.1 M, was used as a supporting electrolyte in which all other reagents were dissolved. Horse spleen ferritin (HoSF type I, Sigma, USA), with approximately 1800 iron atoms per molecule, was used without further purification. It was dissolved in 0.1 M KCl to prepare a stock solution with 100 mg.ml\(^{-1}\) ferritin. Ascorbic acid (AA, Pharmachim, Bulgaria), dissolved in 0.1 M KCl to a concentration of 5.68 mM, was used as an exogenous reducing agent. Cerium disulfate (Ce(SO\(_4\))\(_2\)\(\cdot\)4H\(_2\)O, Merck), dissolved in 0.1 M KCl to a concentration of 0.5 mM, was used as the main titrant. Standardization of the redox titration procedure was performed with iron(II) sulfate heptahydrate FeSO\(_4\)\(\cdot\)7H\(_2\)O (Merck) dissolved in 0.1 M KCl up to a concentration of 1.83 mM. During measurements with ferritin, the solution was buffered to pH 7.4 with 0.1 M phosphate buffer.

2.2. Samples irradiation

Q17 (“Sunnie™”) therapeutic/bactericide device was used as a radiation source. It comprises mercury discharge lamp DRT-230 for UV spectral range (220 nm – 430 nm, \textit{c.a.} 0.5 mW/cm\(^2\)) and halogen lamp for IR (radiates mainly in 0.6 µm – 3 µm, \textit{c.a.} 5 mW/cm\(^2\)). The depicted power density is for a distance of 27.5 cm from the source and the solution surface with the depth \textit{c.a.} 2 cm.

2.3. Redox titration procedure

2.3.1. Instruments

Potentiometric titrations were performed with the setup shown in Fig.1. Ballpoint platinum electrode (OH-09615, Radelkis, Hungary) was used as a working electrode (WE), and double junction Ag/AgCl electrode (OP-0820P, Radelkis) as a reference electrode (RE). Portions of the titrant were deposited to the reaction mixture by a dispenser (Plastomed, Poland). Potential differences between the two electrodes were measured by the potentiometer (N5170, ELWRO, Poland).

2.3.2. Data Processing

Evaluation of the equivalence point of the titration curves was carried out as follows. First, a continuous curve was obtained from the experimental points using Fast Fourier Transform (FFT) Filter Smoothing. Next, first order derivative of this curve was calculated. Finally, the peak of the derivative was obtained. All three steps were performed by using standard algorithms implemented in the software Origin 5.0.

3. RESULTS

3.1. Effects of near infrared radiation on iron mobilization

It was unequivocally shown, that IR-A radiation elicits in cells a signaling response, leading to upregulation of specific proteins. This signal was mediated by an oxidative stress, originating from the respiratory electron transport chain [Schroeder 2007, 28]. The appearance of free radicals in skin upon the irradiation with IR-A was also observed [29]. However, the detailed mechanisms of these phenomena are not well understood. Particularly, although an increased ferritin expression was well...
registered [20], its possible role in the formation of reactive oxygen species (ROS) was not definitely established. Such a “pro-oxidant” ferritin action could be accomplished via Fenton’s reaction with participation of Fe^{2+}, released during eventual reduction of the protein mineral core. While a direct reduction by IR-A is not very likely to occur, other indirect mechanisms cannot be rejected. For example, infrared radiation could be a promoter (due to alterations in protein molecule structure) of the iron efflux caused by chemical agents.

To elucidate this question these questions, the iron mobilization was studied under various conditions of IR-A irradiation. The results are given in Fig.2 and Fig. 3, illustrating the dependence of the titration curves on the duration of irradiation (i.e. dose). Two curves – respectively for 0 and 10 minutes of IR-A exposure are shown.

The curves are measured after incubation of the samples with an exogenous reducing agent (in this case ascorbic acid) following the irradiation. The positions of corresponding equivalence points, determining the amount of reduced iron (Fe^{2+}) in the solution, are obtained by the derivatives of the smoothed experimental data as described earlier [30]. An increase in the quantity of the Fe^{2+} for higher doses is clearly seen.

3.2. Assessment of iron efflux under UV-A irradiation

Not unexpectedly, electromagnetic waves with shorter wavelengths (i.e. higher energies) exerted deeper influence on the ferritin molecule. We observed a prominent efflux of Fe^{2+} upon UV-A irradiation, which is in accordance with earlier results of other authors [26,28]. No exogenous reducing agents were applied in this case, hence such an effect can be ascribed only to a direct photoreduction of the ferritin mineral core. The evaluated amount of released Fe^{2+} was c.a. 5 μmol. The respective titration curve is shown in Fig.4. Given that the total content of ferritin iron in the solution should be 7.2μmol (20μL ferritin x 0.36mol/L iron), the obtained value amounts 69.4%. It is quite a reasonable figure, if we do not expect the whole protein mineral core to be degraded.

4. CONCLUSION

In the present work the effects of UV-A and IR-A irradiation on the ferritin were studied in vitro. The results suggest different mechanisms of action of these two ranges of electromagnetic spectrum. While UV-A is able to induce direct photoreduction of ferric complex inside the ferritin molecule, IR-A seems to exert indirect influence. In the light of above present findings, it is reasonable to assume a role of promoter for this type of radiation which can be viewed as induction of changes in the tertiary and quaternary protein structure.

5. REFERENCES


THE INFLUENCE OF ORIENTATION AND PARTICLE SIZE ON THE INTERFACE FRACUTURE OF A BONE-NANOCOMPOSITE CEMENT

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Abstract – Clinical follow-up studies in cemented total hip arthroplasties found that femoral prosthesis loosening is caused by the fracture of the bone-cement interfaces. The research objectives were to determine whether orientation of the bone has any influence on the interface fracture strength, and to determine whether inclusion of micro/nano sizes MgO particles on Cobalt™ HV bone cement has any influence on the interface fracture strength. Flexural tests were conducted on five groups of specimens to find Young Modulus and bending strength: (1) longitudinal bone, (2) transverse bone, (3) pure cement particles, (4) cement with 36 µm and 27 nm MgO particles, and (5) cement with 27nm MgO particles. Also, fracture tests were conducted on six groups of bone-cement specimen to find interface fracture toughness: (1) longitudinal bone-cement without MgO particles, (2) transverse bone-cement without MgO particles, (3) longitudinal bone-cement with 36 µm MgO particles, (4) transverse bone-cement with 36 µm MgO particles, (5) longitudinal bone-cement with 27 nm MgO particles, and (6) transverse bone-cement with 27 nm MgO particles. Transverse bone specimen was 14% stiffer than longitudinal specimen, while bending strength and fracture toughness of longitudinal specimen was 29% and 2.6 times lower than the transverse specimen, respectively. Reduction of Young’s modulus (7.3%), bending strength (27%) and fracture toughness (16%) was observed by the inclusion of microsize MgO particles, and a reduction of the Young’s Modulus (19%), bending strength (21%), and fracture toughness (19%) for nanosize MgO particles. The interface toughness of the transverse bone infused with 27nm MgO was about 6 times higher than transverse bone infused with 36 µm particles of MgO. Preliminary studies show that orientation of the bone has significant influence on the interface fracture. MgO particles size have a significant effect on the strength of the bone - cement interface.

Keywords – ethanol conservat, cortical bone, fracture toughness

1. INTRODUCTION

Total hip joint replacement is one of the most common orthopaedic surgical procedures along with total knee replacement. The majority of these replacement joints are cemented [4]. The most common problem in cemented total hip arthroplasties is a failure in the interface between the bone and the cement, happening in about 10% of the cases [2]. The addition of small enough particles to fill in the gaps between cement grains might improve the ability of the cement to penetrate into the porous surface of the bone. The bone cement tested in this experiment is a PMMA based high contrast bone cement produced by Cobalt™. The goal of the research is to investigate the effects of microsize and nanosize particles of MgO on the strength of the bone to cement interface. Nanosized particles have had a wide usage as a functional-filling material [3, 5]. Their main advantage is the fact the surface area of a material containing smaller particles is significantly increased, and they have also been known to increase cell function [4, 5]. The increased surface area would then be able to penetrate further into the pores of the bone surface therefore increasing the interfacial strength between the two materials. The fact that bone itself has a naturally adapted compatibility with nano-sized materials, as the hydroxyapatite crystals are 20 to 80 nm long and collagen fibrils are less than 500nm in diameter [5]. The nanoparticle enriched bone cement is a habitable area for osteoblasts to colonize and enable the newly formed bone to fill in the gaps and further tighten the grip to the bone surface [8]. Another advantage of the usage of nanoparticles is the proposed reduction of the temperature in the PMMA exothermic reaction if there are nanoparticles mixed in the cement. This would effectively reduce the damage done to bordering bone cells as the temperatures during PMMA curing can rise up to 80°C [7].

The aforementioned goal was to be achieved first by designing and manufacturing the base and the components necessary to perform a three-point bending test [9], as well as synchronizing the
instrumentation necessary to collect the relevant data. The second objective was to perform tests on all of the materials used, in order to comprehend their elasticity and fracture toughness [1]. The last objective was to perform interfacial strength tests using the previously gathered elasticity and fracture strength data in order to gain a complete view of the properties supplied by the micro and nanosize particles tested. The tests were to be performed on pure bone cement as a control as well as using micro and nanocomposite PMMA. This applied to the elasticity and fracture strength and the interfacial toughness setup.

2. MATERIALS AND METHODS

2.1. Design and manufacture of the setup and instrumentation

The design of the experimental setup was done using SolidWorks™ solid modeling software. Aluminum blocks were used to fabricate the components of the setup (e.g. base, indenter, 3 point bend specimen holder). The parts were manufactured in the UCO Machine Shop using a Bridgeport™ milling machine, band saw and a lathe machine. The primary setup of the base in the SolidWorks model was not accurate enough, and a second take on it was the one used as the dimensions of the load cell screws had to account for the nuts used in order to tighten the indenter onto the load cell itself. A precision xyz stage was assembled with the base for microscopic viewing purposes. The xyz stage was to maintain the whole base on top of a microscope deck, and a piece was designed in order to employ all four holes on the stage while gripping with four screws onto the base so maximum tightness could be achieved. Two rods of high quality aluminum were cut to serve as support for the slider containing the load cell that was going to be pushed by the actuator. The setup as a whole had a flush fit, and there were little adjustments to be made only to make sure the indenter passed unhindered through the hole in the center bar. The aluminum holder for the milling of the bone samples was already made from a previous experiment in the lab, and was used after resurfacing the edges to make sure it was clamped straight on the vice.

The instrumentation consisted of an actuator to facilitate the movement, a load cell to sense the change in the load, and a load cell sensor as an interface to the load cell. The first one of these elements set up was the actuator. It was a Newport™ LTA-HL® actuator. The package included a SMC100, which is a single-axis motion controller, with its appropriate software. The setup and calibration was a very trivial process as the software provided by Newport was enough for the purposes of this experiment and now further research needed to be done. The load cell was a Futek™ LCM300®, item number FSH02630, which is the item number for a 50 lb. model of the particular load cell. It has a capability of sensing compression as well as tension, while also having two threaded screws on both ends which made it perfect for the way the setup was supposed to work. The load cell sensor was a Futek™ IPM500® unit. It had analog output capabilities and a resolution that made it a good match for the load cell. The calibration of the load cell sensor was done using Troemner™ precision weights for electronic calibration. The pre-known forces from the precision weights were used in order to find the calibration coefficient for the sensor, and the result was an accurate load cell reading from pre known non-precision weights borrowed from the general physics laboratories. Figure 1 pictures the final look of the setup.

![Image](Ilik et al.: The Influence of Orientation and Particle Size on the Interface Fracture of a Bone – Nanocomposite Cement)

2.2. Preparing the bone and cement samples

The bone samples were prepared using different apparatus and techniques in the UCO Machine Shop, mainly the band saw and the milling machine. The first step was to get the bovine femurs and use the band saw in order to cut longitudinal samples that were 9 inches long and about 3-5 inches wide. At least two of these were collected per bone, while mainly the band saw and the milling machine. The initial plan included designing a NI LabView™ program to intake the analog inputs fed from the load cell sensor and the actuator and relay that data into a text file with the respective time for each one of the measurements in order to have a fully automated data gathering procedure. The program required to take in the analog input from the sensor was simple and easily finished while fully functioning. On the other hand, the procedure for the setup of the actuator was significantly more complicated, and significant LabView knowledge was needed in order to synchronize it to the specific regulations needed for measuring data. Due to the lack of time in this project this idea was abandoned and it was decided that the data should be gathered manually.
bone was cut using a 4x.012x1/2 in. diamond coated wafering blade to a 20 mm width. The block was sliced every 4 mm to achieve the final dimensions of the samples (20x4x2 mm). To prepare the 20x4x2 mm cement specimen, a 20x4x60 mm mold made out of glass was used to cure the cement. The walls were made to an exact height of 4 mm using an unorthodox method of stacking glass slides that were exactly 1 mm thick on top of each other. The glass slides were perfect as they were accurate as well as smooth enough for the cement not to stick on their walls. A block of bone with dimensions 20x2x30-50 mm (this ranged for the need and availability of bone) was put in the mold, and then bone cement was poured on top of it. This ensured that the thickness of the composite was 4 mm, divided evenly between the bone and cement. Then the samples were cut with the same wafering blade for the final 2 mm dimension. The centre notches were prepared with a 3x0.006x1/2 in. wafering blade, which provided a significantly thinner and clean cut. For the bimaterial specimen, a 20-50x20x2 mm was placed in the same glass mold, and the cement was poured on top and cured under 80 kPa pressure. There were longitudinal and transverse bone specimen made, as shown on Figure 3.

The saline is a highly corrosive substance and a lot of precautions were taken in order to minimize the exposure of saline on the equipment used in the Machine Shop.

![Fig. 2 – Milling Process](image)

2.3. Conducting the tests

The tests were conducted using the previously shown setup. A micro-level actuator was moving at a velocity of 11 µm/s in order to minimize the load iterations for abundant amounts of data. The actuator pushed a load cell that was connected to the indenter which was acting as the loading in the three point bending system. Readings were taken from the load cell as the actuator stopped to give some relaxation time to the samples. The time iterations for the data points taken varied from materials used, as the cement with micro and nano particles tests took about 10 minutes, while pure longitudinal and transverse bone took only about 5 minutes. The force was read only on the linear portion of the force versus point load displacement graph during the Young’s Modulus of Elasticity readings. This was confirmed by a very consistent correlation coefficient on each one of the trials. The tests for the Young’s Modulus and Flexural Strength were done on specimens that were simply fitting the 20x4x2 mm dimensions. The tests for Fracture Strength were done using specimens that were the same dimension, but had a center notch to initiate the crack that went 2 mm deep. The samples for interfacial strength were done on bone-bone cement specimen that had a center notch that cut through the bone cement, which is once again half way through the specimen. During the testing the live bone samples were continuously kept moist using deionized water, as saline was too corrosive for the specimen holder. The tests themselves took only about 5-10 minutes, with the live bone samples taking only about 5-6 minutes, which doesn’t allow enough time for the osteocytes to die.

3. RESULTS

The results from the Young’s Modulus of Elasticity and Flexural Strength were around the expected value for the pure bone samples. Transverse cracks were significantly harder to initiate and the bone was also significantly stiffer than the longitudinal bone. This is illustrated by the fact that transverse bone had a 14% higher Young’s Modulus, while the flexural strength was 29% higher. The pure bone cement and its mixtures all had a similar change in these parameters to the bone. A trend of increasing elasticity as smaller particles were added was observed, while the materials themselves were significantly more elastic than bone. The Flexural Strength provided more
Ilik et al.: The Influence of Orientation and Particle Size on the Interface Fracture of a Bone – Nanocomposite Cement

scattered data rather than the very consistent Young’s Modulus data. The Flexural Strength was lower in the bone cements, although the pure bone cement was not significantly weaker than the longitudinal bone sample. Nevertheless there was a drop of 27% in the bending strength with the addition of microsize MgO particles in the bone cement. The addition of nano had an insignificant rise in the Flexural Strength from the microsize MgO particles. For the pure bone cement tests there were two different specimen used. Two of the samples were cured under 60 kPa rather then 80 kPa which was the case for all of the other bone cements used. These two specimen that were cured under less pressure had almost double the Young’s Modulus of Elasticity and a 35% higher Flexural Strength. The Young’s Modulus data is presented on Figure 5, while the Flexural Strength is on Figure 6.

For the Fracture Toughness data there was only the transverse center notch bone that had a significantly higher breaking point, while all of the other categories were in the same vicinity, with none differing significantly from the other. While their actual forces on which the bone broke was different, the calculated Fracture Toughness was very similar as shown on Figure 7. During the preparation of the specimen of bone cement with microsize MgO particles there was a mishap as the thin blade that was used to prepare the center notches broke, and the thicker blade was used to prepare the last two center notches. This allowed for an unplanned test on the notch effect, which is the effect of the size and quality of the centre notch in the crack initiation. The last two bones came out to be very close, considering the amount of test samples ran, as a percent difference of 12% was calculated.

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The method of preparing the Interfacial Toughness bones seemed to be working well in the preliminary tests whenever dead bone was used (the samples weren’t immersed in saline water). During the center notch preparation of the final specimen (the samples were totally moist throughout the process) the bone to bone cement interface failed from the pressure of the wafering blade saw clamp. In order to try to preserve at least a few specimens, they were clamped very lightly which led to the mishap of breaking the thinner 3x0.006x1/2 in. wafering blade mentioned previously. Nevertheless, three samples remained intact and were mounted on the specimen holder to perform the Interfacial Toughness test. Two of those were with bone cement with microsize and one with nanosize MgO. Although the data is not statistically relevant the Interfacial Toughness was very different between the different sized particles. The addition of nano, rather than microparticles increased the strength of the interface 6 times (Figure 8).

The different types of bone cement surfaces were observed on a fluorescence microscope provided by the UCO Biology Department. Using a power of 100x and green light surface pictures were taken so the materials could be examined closely. All three types of bone cement sample pictures are presented on Figure 9.
4. CONCLUSION

Material properties vary with the orientation of the bone. The transverse bone was always notably stronger and less elastic than longitudinal bone. This result is exactly what was expected because of the osteon positioning which is lengthwise in bone. Breaking each one of them requires more force than breaking the connections from the Haversian canals as it would be in longitudinal bone. The cement samples were all considerably weaker as well as more elastic than any of the bones. The fact that bone cement is more elastic than bone means that it can absorb a lot more energy before breaking, and is able to deform a lot more than bone. Because it is less brittle the bone cement is less keen on fracturing, as a large deformation is needed in order to shatter the bone cement. During the course of experiment the indenter went about 1.3 mm into the bone cement before the crack initiated. This means that a severe deformation is needed in order to fracture the cement, which makes it very reliable for its purpose. The micro particles lowered the elasticity of the cement, while the nano particles seemed to lessen the drop in flexural strength. Nevertheless, none of these properties had any significant changes from the addition of nano and microsize MgO particles. Filling out the small gaps between the bone cement granules with smaller sized MgO particles was supposed to make the material less brittle, and that did happen, as shown on Figure 10, the deformation due to the force needed to be slightly larger in order to initiate a crack in the modified materials. But these differences are not statistically relevant as the values are close to each other. Another aspect that was investigated was the curing pressure effect. The cement cured under 60 kPa was significantly stronger, as well as more brittle than the bone cement cured under 80 kPa. This result makes sense, as more pressure would press the bone cement particles closer to each other, making the network of particles more elastic. The fact that the network is more elastic means that it also breaks sooner, as illustrated by the 35% lower Flexural Strength.
than the other ones, but enough to go out of the standard deviation boundaries. Another aspect that was tested during the Fracture Toughness was the notch effect. While using a thicker 4x.012x 1/2 in. diamond coated wafering blade, rather than the thinner 3x.006x 1/2 in. wafering blade, the loads at which the crack initiated were taken. As the data showed there was not a significantly different trend in these specimens tested. Therefore these bone cement samples were also included in the final data presented. This was tested on bone cement with 36 μm MgO particles only, but the presence of different materials does not concern the notch effect.

The surface view provided by the fluorescence microscope didn’t provide significant insight into its properties. A smoother surface can be observed on Figure 10. B and C, as the smaller granules penetrated within the spots of the separate PMMA granules. A transmission electron microscope or a scanning electron microscope view would provide a better picture about the surface structure of the different bone cement composites [3].

There weren’t enough data gathered to investigate the role of nano particle addition on interfacial strength with statistical significance, but the limited data showed a substantial increase. The specimens were prepared using the method specified in the Materials and Methods section, and as the procedure suggests, a 4 mm thick plate of bone and bone cement connected was clamped to the wafering blade saw, and the final 2 mm dimension was cut. While doing this final cut, the pressure from the clamp itself broke the bone to the side. While trying to adjust the pressure of the clamp between the breaking point and a very loose bone cement bond, making the cement part move to the side. The main problem encountered in this project was the bone to bone cement interface issue while clamping the specimen into the wafering blade saw. A probable cause for the bone to cement interface failure might be the fact that the samples were immersed in saline water for 12 hours prior to testing, and frozen to preserve the bone integrity to a maximum level. While doing the tests on the preliminary specimens, which were not considered in the final data, the bones were never frozen and there were no failures in the bone to bone cement interface prior to the testing. Another approach might be changing the whole clamping system on the wafering blade saw, which would involve machining a new piece that will be more compatible with the bone samples, by not applying that much pressure while holding the specimen in place.

5. REFERENCES

6. APPENDIX

Equations:

Young’s Modulus: \[ E = \frac{P_l^3}{4tw\delta_{LP}} \]

Flexural Strength: \[ \sigma_f = \frac{3P_{max}l}{2tw^2} \]

Fracture Toughness: \[ K_{IC} = \left[ \frac{P_{max}l}{tw^{3/2}} \right] \ast f\left( \frac{a}{w} \right) \]

\[ f\left( \frac{a}{w} \right) = \frac{3\left( \frac{a}{w} \right)^2}{2} \left[ 1.99 - \left( \frac{a}{w} \right) \left( 1 - \left( \frac{a}{w} \right) \right) \left( 2.15 - 3.93\left( \frac{a}{w} \right) + 2.7\left( \frac{a^2}{w^2} \right) \right) \right] \]

Interfacial Toughness: \[ G = \frac{P_{max}^2}{8Et} \left( \frac{1}{I_C} - \frac{1}{I_S} \right) (l - a)^2 \]

where IC and IS are:

\[ I_C = \frac{1}{12} tw^3 \]

\[ I_S = \frac{1}{12} tw_C^3 \]

Legend:

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>(l)</td>
<td>1.6 mm, length of the lower two points in the 3point bending system</td>
</tr>
<tr>
<td>(t)</td>
<td>the thickness of the sample, around 2 mm</td>
</tr>
<tr>
<td>(w)</td>
<td>the width of the sample, around 4 mm</td>
</tr>
<tr>
<td>(P/\delta_{LP})</td>
<td>the slope of the straight line portion of a load versus displacement graph</td>
</tr>
<tr>
<td>(P_{max})</td>
<td>the load that causes the crack initiation</td>
</tr>
<tr>
<td>(w_C)</td>
<td>the height of the cement portion of the composite specimens</td>
</tr>
</tbody>
</table>
THEORETICAL MODEL FOR THE UV DISINFECTION SYSTEM IN THE OPERATING WARD OF PZU “FILIP VTORI”

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Abstract – Here we investigate the theoretical modeling of an UV disinfection system for the operating ward in PZU "FILIP VTORI". As nosocomial infections pose a serious threat to patients everywhere in the world, here the disinfection of the air and the surfaces is modeled and discussed. The surfaces are disinfected with direct illumination of open UV after hours system, UV curtains, overhead disinfection, floor disinfection and disinfection of the incoming air through the ventilation/air-condition system. From the results it can be seen that the concentrations of bacteria, fungi and viruses drop significantly which in turn should give a significant drop in a number of hospital acquired infections.

Keywords – UVGI, infections, disinfection, operating room

1. INTRODUCTION

UV disinfection has been a method for disinfecting air, surfaces and water for quite a while. Lately disinfection methods for disinfection of raw foods have been developed. Primarily for the disinfection of raw meat and clear juices through irradiation from xenon pulsing light lamps [1]. The disinfection of microorganisms is conveyed through the dimerisation of thymine in the DNA [2]. The DNA has a very narrow band of resonance frequencies which coincides with one of the highest spectral lines of excited mercury under low pressure. The spectral line of mercury is at 253.7nm. The lamps that produce this spectral line are called low pressure mercury lamps. There are also medium pressure lamps and xenon pulse lamps. All three have different applications and properties.

2. MATERIALS AND METHODS

In this project we use modeling software and also the general mathematical package Mathematica™ 7.0 by Wolfram Research. The modeling software is DIALux™ 4.8.0.1 by DIAL, GmbH, Lüdenscheid. DIALux™ is primarily used for lighting picture rendering and the primary unit of measurement there is lux. But since lux is a unit of measurement which is tied to the human sense of sight it is of no purpose in the world of UV light where the used unit of measurement is W/m². Because of this, DIALux™ is used only for qualitative investigation. Namely, when a simulation is done it is used so that no shadows are created, nor large discrepancies in the irradiation field strength.

Fig.1 Germicidal efficiency of UV wavelengths, comparing High (or medium) and Low pressure. UV lamps with germicidal effectiveness for E. coli. Based on data from Luckiesh (1946) and IESNA (2000)

In the course of this research a small Mathematica™ 7.0 notebook was created which was used to calculate the irradiances at arbitrary spots on the surfaces and in the air when needed. The code is given below together with the explanation of the formulas used.
**Proceedings of the Second Conference on Medical Physics and Biomedical Engineering**

The constant dol is the length of the arc inside the tube; \( x \) is the distance from the middle of the tube; \( r \) is the radius of the tube; \( E_{uv} \) is the power of the tube given in pure UVC watts; \( I_{uv} \) is the irradiance of the UVC on a perpendicular element at some distance \( x \) from the middle of the tube. This is the most important number used when calculating the survival rate of a particular microorganism.

To calculate the survival rate of a particular microorganism a constant for that microorganism must be known. For most of them these numbers can be found in reference tables. This constant is called UV rate constant, \( k \), and its unit of measurement is \( \text{m}^2/\text{J} \). The survival rate, \( S \), is given by the formula

\[
S = e^{-kD}
\]

(1)

where \( D \) is the integrated UVC dose over some time. Considering that variations in the UVC output are very slow, instead of integrating we simply multiply the irradiance with the time to obtain the dose, as such

\[
D = t \cdot I_{uv}
\]

(2)

The extinction rate, \( R \), is simply

\[
R = 1 - S
\]

(3)

These are all the methods and formulas that we need to model the UV disinfection system for almost any space.

### 3. RESULTS

#### 3.1 Direct UV irradiation of rooms

The results given here will be for the spot that is in the middle of each room respectively. There is an extensive list of measured UV rate constants for almost all known or important microorganism from which averages have been drawn [2]. From these average values we determine the extinction rates for each room and each microorganism group separately. If any extinction value falls under \( \log_{10} \) it is automatically equaled to 100%. This method gave extinction rates for each room that were greater than \( \log_{10} \). Since all of the numbers were 100% in consideration we put representatives from each microorganism group that are the most resistant to UV for that group. It must be noted that the method used is the one for the worst case scenario. By this it is meant that the reflectivity of the surfaces are taken to be the ones for UV, not visible light. If a reflectivity constant for some surface is unknown then it is taken to be 0%. Using this method we get numbers that are the worst that can happen. The extinction percentages are the lowest theoretically possible. In practice this means that the numbers can only be higher than these given here, thus ensuring at least the lowest known rate of extinction. The numbers were calculated for 6 hours of irradiation and are given in Table 1. The layout plan of the operating ward is given in Figure 2. On the layout plan the relative irradiances are given together with the distribution of the lamps.

**Fig. 2 - Layout plan of the operating ward**

#### 3.2 Disinfection of in-duct air

The air that enters the operating ward is supplied by a ventilation system. This system gives a positive pressure of the air inside versus the air inside, so no air from outside can contaminate the premises. In turn the air that is supplied through the ventilation system is only treated with HEPA filters which have very good results in removing micro particles. To ensure a better disinfection of the air UV disinfection system is modeled for the intake air. The lamps in this case are medium pressure mercury lamps.
There are three intake ducts. The first one supplies air at a rate of 5200 m³/h, the second and the third one supply 7300 m³/h. Their lengths are 1.7 m, 1.3 m and 1 m respectively. Their perpendicular dimensions are 0.35 m x 0.7 m, 0.4 m x 0.7 m and 0.4 m x 0.7 m respectively. A calculation is needed to ensure that the UV rating of these ducts is at least 20.

The exposure time of the air in each duct can be calculated through the following formula:

\[ t = \frac{WHL}{Q} \]  

(4)

where

- \( W \) is the width
- \( H \) is the height
- \( L \) is the length
- \( Q \) is the rate of air supply

The exposure times for the three ducts are

- \( t_1 = 0.29 \text{s} \)
- \( t_2 = 0.18 \text{s} \)
- \( t_3 = 0.14 \text{s} \)

The total irradiance is calculated with reflectivity of the internal walls of 50%.

The total irradiance is

\[ I_{\text{rtot}} = I_{R1} + I_{R2} + I_{R3} + \left( \frac{I_{R1} I_{R2} I_{R3}}{(I_{R2} - I_{R3})^2} \right) \]  

(5)

Using formula (6) to calculate the view factor for each reflection separately, for 1000W PHILIPS HOK 10/120L lamp it yields:

\[ F = \frac{L}{\pi H} \left( \frac{1}{L} \arctan \left( \frac{L}{\sqrt{H^2 - 1}} \right) + \frac{Z - 2H}{\sqrt{ZY}} \arctan \right) \]  

(6)

\[ I_{\text{tot1}} = 3329.68 \text{ W/m}^2 \]
\[ I_{\text{tot2}} = 6659.36 \text{ W/m}^2 \]
\[ I_{\text{tot3}} = 6659.36 \text{ W/m}^2 \]

for each duct separately. It should be noted that the first duct has one lamp and the second and third have two lamps. The lamps are positioned perpendicular to the air flow.

Considering the exposure times for each duct the dose can be calculated.

\[ D_1 = 965.6 \text{ J/m}^2 \]
\[ D_2 = 1198.68 \text{ J/m}^2 \]
\[ D_3 = 932.31 \text{ J/m}^2 \]

These dose rates easily put this system in the highest possible UV rating of UVR=24

### 3.3 Upper room air disinfection

Upper room air disinfection is utilized in ultra high clean rooms like operating rooms which are the subject of our investigation. Due to the fact that the light is parallel to the ceiling and the systems are mounted above 2.7 meters there is no harm to the personnel working in the room. They are used to continuously disinfect the air for the whole time while personnel is present. The air circulates due to convection so even if new contaminants are introduced to the room they will pass through the disinfection sector of the room.

Presently there are no guidelines for calculation of extinction rates of these systems and they are installed one in each room. The lamp inside is the standard 36W low pressure mercury lamp.

### 3.4 UV Curtains

UV curtains are installed above doors to create a wall of UV light that will ensure extinction of microorganisms that enter the room when the door is opened. Due to the fact that people passing the doors never stay in the UV light more than 0.5 seconds there is no need for extra protective measures for the eyes and the skin. Additionally, this means that nobody should stay under the doorframe for no particular reason. If one intends to do so, the curtain should be turned off.

Similarly to upper room systems, presently there are no guidelines for calculation of extinction rates of these systems and they are installed one in each room. The lamp inside is the standard 36W low pressure mercury lamp.

### 4. CONCLUSION

From the given investigation it can be seen that with the installation of properly designed UV disinfection systems concentrations of bacteria, viruses and fungi can be severely reduced. Parallel to this reduction of bacterial counts goes the reduction of hospital acquired infections which pose a serious problem not just for hospitals in third world countries but also for those in well developed countries.
Another benefit of these systems is the fact that usage of disinfection chemicals is greatly reduced and the power consumption is minimal.

5. REFERENCES


SOFTWARE APPLICATION FOR QUALITY CONTROL PROTOCOL OF MAMMOGRAPHY SYSTEMS

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Abstract – Considering the fact that the Quality Control of the technological process of the mammographic system involves testing of a large number of parameters, it is clearly evident that there is a need for using the information technology for gathering, processing and storing of all the parameters that are result of this process. The main goal of this software application is facilitation and automation of the gathering, processing, storing and presenting process of the data related to the qualification of the physical and technical parameters during the quality control of the technological process of the mammographic system.

The software application along with its user interface and database has been made with the Microsoft Access 2003 application which is part of the Microsoft Office 2003 software packet and has been chosen as a platform for developing because it is the most commonly used office application today among the computer users in the country. This is important because it will provide the end users a familiar environment to work in, without the need for additional training and improving the computer skills that they posses.

Most importantly, the software application is easy to use, fast in calculating the parameters needed and it is an excellent way to store and display the results. There is a possibility for up scaling this software solution so it can be used by many different users at the same time over the Internet. It is highly recommended that this system is implemented as soon as possible in the quality control process of the mammographic systems due to its many advantages.

Keywords – FTIR software, mammography, Quality Control

1. INTRODUCTION

A prerequisite for a successful screening project is that the mammograms contain sufficient diagnostic information to be able to detect breast cancer, using as low a radiation dose as is reasonably achievable (ALARA). This quality demand holds for every single mammogram. Therefore, Quality Control must ascertain that the equipment performs at a constant high quality level [1-3].

Considering the fact that the quality control process involves testing a great number of parameters, it becomes obvious that there is a need for implementing an IT solution for gathering, processing and storing all the data which come out of this process. Therefore, this software application was developed. It consists of a user interface and a database, both written and developed in Microsoft Access 2003, as a platform (program) that is most commonly used among computer users in our country today. The goal is to enable all users, even those with limited computer skills, to use the software application without the need for further education and training.

The database is comprised of 16 tables, 6 queries, 4 user interfaces and 2 types of reports. In each table there are data fields in which data are entered through the user interfaces. In the user interfaces, the data fields are organized following a scheme that is needed to run a successful quality control process. The parameters are organized in groups, which are properly marked, easy to understand and that minimizes the risk of writing parameter values at a wrong place. This is done so that the user can quickly adapt to the user interface and follow it just like he/she would follow a paper scheme for entering the gathered data. Throughout the application, there are buttons which offer different functionalities which will be discussed later on.
The queries are used for displaying the data fields on the user interface forms, as well as for storing the inputted data into the database tables.

The following figure displays the main menu of the application.

![Main menu of the application](image)

**Fig. 1 – Main menu of the application**

### 2. MAIN MANU

As can be seen on Figure 1, there are 4 buttons. By clicking on the first button, the user can start with the gathered data input process. The second button can be used to get into preview / correction mode, meaning that the user can take a look at the previously entered data and make corrections if necessary. Once a value is entered into a field, it automatically gets stored in the database and can be reviewed and/or corrected using the user interface. There is no need for saving the data, which means that if the computer fails, the data won’t be lost.

The third button takes the user to the Reference values panel of the application. This part is reserved for parameter values that are constant (according to the European Protocol for Quality Control of the Mammography Systems) [1], but used in different calculations. However, if there is a need to change these fixed values (for example due to a policy or regulation change), the reference values can be changed in this section of the application. Modifying or deleting the reference values in the data input interface is not allowed.

The fourth button is used for exiting the application.

### 3. DATA INPUT USER INTERFACE

The data input user interface is shown on Figure 2.

![Data input user interface](image)

**Fig. 2 – Data input user interface**

The data input fields are organized in tabs which contribute to better clarity. Each tab contains the testing parameters which fall under specific category. The navigation between the data input fields is very easy by using the Tab key, which leads the user through the scheme in the right order. The button “Прегледај ги резултатите за овој запис” is enabled on the first tab in the data review mode of the application. That button is used to quickly navigate to the results part of the application.

On the last tab, “Плоча за магнификација”, which is shown on figure 3, there are two buttons which lead the user to the next part of the application. The first button is for continuing with the data input process, and the second button is for continuing with the review / correction procedure, depending on the mode in which the user has started the application (data input or data review, respectively). It is important to emphasize that if the application is in data input mode, the second button is disabled and vice versa.

![“Плоча за магнификација” tab](image)

**Fig. 3 – “Плоча за магнификација” tab**

The second part of the application is displayed on the following figure.

![Second part of the application](image)

**Fig. 4 – Second part of the application**

Across all the tabs, on the right side of the user interface, the period after which the tests should be conducted again is shown with red text. The time periods are written according to the European Protocol for Quality Control of the Mammography Process [4, 5].
4. RESULTS SECTION

When the data input process is complete, the user can navigate to the results section of the application, which is shown on the next figure.

![Results section](image)

As Figure 5 shows, a large number of parameters are being tested. For every parameter or parameter group there is a dedicated button which carries-on the test. Right next to the button, in a label, the result of the calculation (test) is being displayed, followed by the referent (allowed) value of the parameter according to the European Protocol and finally, in the last label the final result is shown, represented by the words “Задоволува” if the calculated parameter is within the given limits, and “Не задоволува” if the value is outside the limits given by the European Protocol.

There is a large text field in the bottom of the form which can be used to write a report or a few remarks considering the testing process by the person who conducted the quality control procedure.

When the testing and calculating process is over, the measured values and received results can be displayed in Reports which are given to the person / organization which ordered the testing of their equipment.

There are two types of reports: brief report and complete report. The brief report, on one page, shows the most important specifications of the equipment tested as well as the most important parameters which are part of the Quality Control process.

The full (complete) report consists of seven pages where all the measured and tested values and parameters are shown. These two reports can be easily printed out and handed over in a hard copy version.

By clicking on the last button on the results page, the data input user interface closes and the user is taken back to the main menu, from where he/she can start over with a new set of measures taken during the Quality Control process, or the user can review and/or correct an already entered set of values.

The following figure describes the structural and functional scheme of the application.

![Structural scheme of the application](image)
5. CONCLUSION

This application offers an easy, precise and effective way of handling the gathered Quality Control data and it is highly recommended that this system is implemented as soon as possible in the quality control process of the mammographic systems everywhere where this types of tests are conducted.

6. REFERENCES


