

Verifying the accuracy of dose distribution in Gamma Knife unit in presence of inhomogeneities using PAGAT polymer gel dosimeter and MC simulation

T. Allahverdi Pourfallah^{1*}, M. Allahverdi¹, N. Riyahi Alam¹, M.R. Ay^{1,2}, M.H. Zahmatkesh³

¹Department of Medical Physics and Biomedical Engineering, Tehran University of Medical Sciences, Tehran, Iran

²Research Center for Science and Technology in Medicine, Tehran University of Medical Sciences, Tehran, Iran

³Novin Medical Radiation Institute, Tehran, Iran

Background: Polymer gel dosimetry is still the only dosimetry method for direct measuring of three-dimensional dose distributions. MRI Polymer gel dosimeters are tissue equivalent and can act as a phantom material. In this study the obtained isodose maps with PAGAT polymer gel dosimeter were compared to those calculated with EGSnrc for single-shot irradiations of 8 and 18 mm collimators of Gamma Knife (GK) unit in homogeneous and inhomogeneous phantoms. **Materials and Methods:** A custom-built, 16 cm diameter spherical Plexiglas head phantom was. Inside the phantom, there was one cubic cutout for insertion of gel phantoms, and another cutout for inserting the inhomogeneities. The phantoms were scanned with a Siemens clinical 1.5 T MRI scanner. The multiple spin-echo sequence with 32 echoes was used for the MRI scans. **Results:** The results of measurement and simulation in homogeneous and inhomogeneous phantoms showed that the presence of inhomogeneities in head phantom could cause spatial uncertainty higher than ± 2 mm and dose uncertainty higher than 7%. **Conclusion:** the presence of inhomogeneities could cause dose differences which were not in accordance with accuracy in treatment with GK radiosurgery. Moreover, the findings of Monte Carlo calculation revealed that the applied simulation code (EGSnrc) was a proper tool for evaluation of 3D dose distribution in GK unit. *Iran. J. Radiat. Res., 2009; 7 (1): 49-56*

Keywords: Gamma knife, PAGAT gel dosimeter, EGSnrc, dose distribution.

INTRODUCTION

Stereotactic Gamma Knife (GK) radiosurgery plays an important role in managing small intracranial brain lesions of volume typically less than 25 cm³ (1, 2). The

efficiency of the technique is based on the high precision delivery of a therapeutic radiation dose to the target employing a steep dose gradient in all three dimensions, which facilitates restriction of the dose to the surrounding normal tissues within the accepted tolerance levels. 201 ⁶⁰Co beams intersecting at the so-called unit centre point (UCP), and four helmets with different collimators size, form four standard clinical beam sizes of 18, 14, 8 and 4 mm nominal diameter.

Currently, polymer gel dosimetry is still the only dosimetry method for directly measuring three-dimensional dose distributions. Polymer gel dosimetry is a technique that has the ability to map absorbed radiation dose distributions in three dimensions (3D) with a high spatial resolution. Polymer gel dosimeters offer a number of advantages over the traditional dosimeters such as ionization chambers, thermoluminescent dosimeters (TLD) and radiographic films. The advantages include independence of radiation direction, integration of dose for a number of sequential treatment fields, and perhaps most significantly, evaluation of a complete volume at once. Polymer gel

*Corresponding author:

Dr. Tayyeb Allahverdi Pourfallah,
Department of Medical Physics and Biomedical Engineering, Tehran University of Medical Sciences, Tehran, Iran.

Fax: +98 21 88973653

E-mail: tallahvardi@razi.tums.ac.ir

dosimeters are tissue equivalent and can act as a phantom material^(3, 4).

Several reviews on the polymer gel dosimetry systems have been presented previously⁽⁵⁻⁸⁾.

In this study the PAGAT (polyacrylamide gelatine (PAG) And THPC anti-oxidant) gel dosimeter was used to investigate the effects of air and PTFE (Poly-tetra-fluoro-ethylene) inhomogeneities on dose delivery accuracy of GK systems.

In the investigation of dose perturbations produced by heterogeneities, Monte Carlo has proved to be a useful tool. The degree of accuracy that can be attained by MC simulation is determined mainly by the following factors:

- The accuracy of the cross-section data used for simulating the various interactions between the ionizing radiations and matter.
- How accurately the radiation beams are modeled with respect to energy and angular distribution.
- The statistical accuracy of the Monte Carlo calculation is mainly determined by the number of histories simulated and the consequent implications for simulation time.
- How the phantom geometry and tissue properties are related to the radiation interaction that are modeled.

Some studies examined the shot placement accuracy of Gamma Knife units by measuring dose distribution or measuring the distance between the location of the maximum dose and the mechanical center⁽⁹⁻¹¹⁾. Comparison of 1D line profiles and 2D dose distributions between measurements and LGP (Leksell Gamma Plan) calculations was undertaken by some investigators⁽¹¹⁻¹⁵⁾. Several studies have been performed to investigate the effects of inhomogeneities on dose distribution using MC simulation along with conventional dosimeters⁽¹⁶⁻¹⁹⁾, however, investigation of effects of inhomogeneities on dose distribution along three coordinate axes using polymer gel dosimeter along with MC simulation are rare⁽²⁰⁾.

Verification of 2D dose map in a single

shot irradiation with 8 and 18 mm collimators in treatment with GK unit in presence of air and PTFE inhomogeneities using simulation and measurement are the purpose of this study.

MATERIALS AND METHODS

Gel preparation and phantom design

In this study PAGAT polymer gel dosimeter was fabricated according to composition proposed by Venning *et al.*⁽²¹⁾ who noted using MRI. The formulation to give the maximum change in the transverse relaxation rate R_2 was determined to be 4.5% *N,N'*-methylene-bis-acrylamide (bis), 4.5% acrylamide (AA), 5% gelatine, 5 mM Tetrakis-phosphonium chloride (THPC), 0.01 mM hydroquinone (HQ) and 86% ultra-pure de-ionized water.

To fabricate the gel dosimeter, the De Deene *et al.*⁽²²⁾ proposed method was used in which the AA and bis were dissolved in the 40% total water volume by heating to 45 °C, using an electrical heating plate controlled by a thermostat. Then the gelatin (300 Bloom) was cooled down to 35 °C before it was mixed with the monomer solution. The antioxidant and HQ were added to the solution under heavy stirring just before filling the test tubes and gel cubes.

The fabrication procedure according to Venning *et al.*⁽²¹⁾ method is somewhat different from De Deen's *et al.*⁽²²⁾ method, in which the gelatine was added to the water and left to soak for 10 min, followed by heating to 48 °C. Once the gelatine was completely dissolved the heat was turned off and the cross-linking agent bis was added and stirred until dissolved. Once the process was completed, the AA was added and stirred until dissolved. Using pipettes, polymerization inhibitor HQ and the THPC anti-oxidant were combined with the polymer gel solution.

The vials and gel cubes were sealed with Teflon lined screw top caps. Upon completion of manufacture, the polymer gels were stored in a refrigerator maintained at

4 °C.

Phantom in this study was a 16cm spherical Plexiglas in which there was a cubic cutout for inserting the gel vials ($4 \times 4 \times 4 \text{ cm}^3$), and another one ($4 \times 4 \times 3 \text{ cm}^3$) for inserting the air and/or a bone equivalent material [Poly-tetra-fluoro-ethylene (PTFE), with density of 2.2 gm/cm^3].

Irradiation of phantom and calibration tubes

The Leksell stereotactic frame was attached to phantom via fastening the four fixation screws on pre-determined phantom positions to ensure reproducibility, and the alignment of the reference coordinate system with the stereotactic coordinate system of the GK (Elekta, Sweden) unit.

The reproducibility of the above procedure obviates the need for imaging each individual gel cube independently with the stereotactic frame attached to it for the purpose of planning the irradiations. Therefore, a series of Computed Tomography (CT) images acquired in a single imaging session of a gel phantom-stereotactic frame assembly were imported to the LGP treatment planning system (TPS) software to plan three different irradiations. Three gel cubes were irradiated using single shots with the 8 mm and 18 mm collimator helmets respectively to deliver a maximum dose of 40 Gy, in two separate experiments.

Figure 1 shows the phantom placed in a Gamma Knife unit (model 4C) for irradiation

tion. The calibration tubes were irradiated using the Theratron Co-60 machine (Theratronics, Ontario, Canada), using a special container in which the calibration vials could have been located horizontally. The calibration vials were irradiated from 0 to 50 Gy with steps of 2.5 and 5 (i.e., 0, 2.5, 5, 10, 15, 20, 25, 30, 35, 40, 45 and 50). Post-manufacture irradiation time was 24 hours.

Gel evaluation

Because of high dose response sensitivity, the MRI was chosen as a readout device. The phantom was imaged, using a clinical 1.5 T Siemens MRI scanner (Symphony, Germany) in the transmitter/receiver head coil. A multi-echo sequence with 32 echoes was used for the evaluation of irradiated polymer-gel dosimeters. The parameters of the sequence were as follows: TR 5900 ms, TE 22–640 ms, slice thickness 1 mm, field of view (FOV) 128 mm, percent phase FOV 75%, matrix size 256×192 , matrix size 256×256 , pixel size $0.5 \times 0.5 \text{ mm}^2$, and one acquisition. The R_2 ($1/T_2$, spin lattice relaxation rate) maps were computed using modified radiotherapy gel dosimetry image processing software coded in Mat. Lab⁽²³⁾. Calibration data for the PAGAT gel batch used in this work were derived by the analysis of axial R_2 maps of the calibration gel tubes 24 hours post-irradiation and a quadratic fit was performed on R_2 values of PAGAT in the dose region of 0-45 and 0-50 for experiment with 8 mm and 18 mm

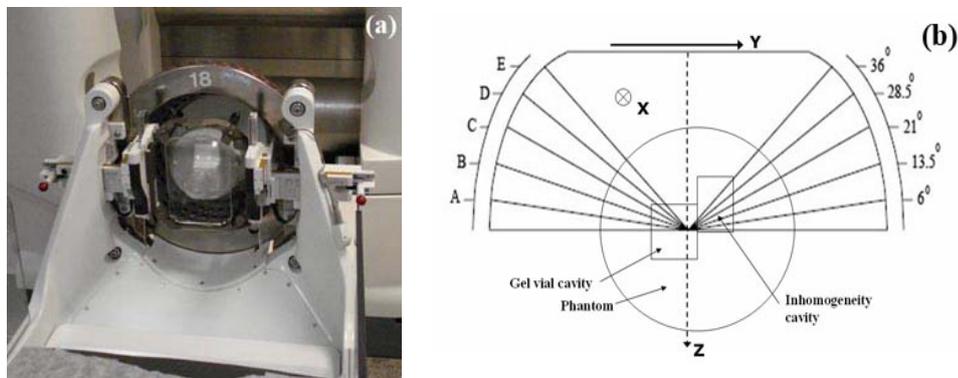


Figure 1. Phantom placed in a Gamma Knife unit (model 4C) for irradiation (a) and the schematic view of the irradiation experimental set-up for the 8 and 18 mm collimator helmet (b).

collimators, respectively figure 2. Post-irradiation imaging time was also 24 hours. The data points corresponded to the average R2 values for each vial in the region of interest (ROI) irradiated in the dose range 0-45 Gy, and the error bars to the standard deviation of the R2 values (σ_{cal})⁽²⁴⁾.

Due to oxygen effect in dose ranges up to 5 Gy, dose response for the applied fabrication method was very little. However, by increasing the concentration of THPC, dose response was observed for doses lower than 2.5 Gy⁽²⁵⁾.

The R2 matrix was subsequently converted into a relative dose matrix, normalized to the maximum prescribed dose of 40 Gy.

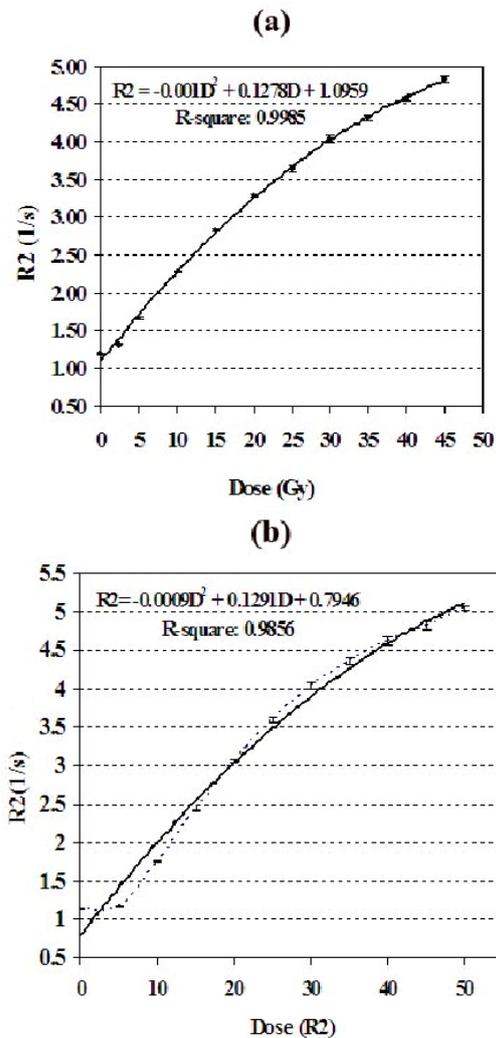


Figure 2. R2-dose curve of PAGAT polymer gel dosimeter for 8 mm (a) and 18 mm collimators of GK unit (b).

Monte Carlo modeling

EGSnrcMP simulation code⁽²⁶⁾ was used to investigate the accuracy of polymer gel dosimetry in presence of inhomogeneity.

The EGSnrc-based MC user code BEAMnrc^(27, 28) was used to simulate the geometry of the GK source channel, and the outputs phase-space data (phase-space files), which included all the particle information (i.e., the charge, position, direction, energy and history tag for each particle). Another general-purpose MC EGSnrc user code DOSXYZnrc^(28, 29), which considers the phantom divided in a large number of small volume elements, or voxels, was employed to obtain the 3D dose distributions in the phantom.

In this study, the simplified source model was employed to permit the researchers to substitute the full source channel by a point source, and the configuration source was situated at the centre of the active core of the GK source, which emitted, its defined photons inside the cone, and the output helmet collimators whose aperture for 18 mm collimator was 2.57 degree⁽³⁰⁾. This simplified model produced doses in agreement with those found with full geometry of the source channel⁽³¹⁾.

The cut-off energies on BEAMnrc simulation were 100 keV for electrons and 10 keV for photons. The maximum step size for electron transport was 5 cm and the number of histories for this run was 6×10^8 .

The cut-off energies on DOSXYZnrc were the same as those on BEAMnrc, but the number of histories in this case was 8×10^8 .

RESULTS

To verify the accuracy of the applied code, LGP prediction was used in homogeneous phantom for a single shot irradiation of GK unit with 18 mm collimator.

Figure 3 compares the LGP predicted relative dose profile along X-axis with MC simulation. Average dose difference between simulation and LGP prediction in flat area

(low dose gradient) of dose profile was lower than 1%, and in steep dose gradient region, distance to agreement (DTA) on average was lower than 1 mm.

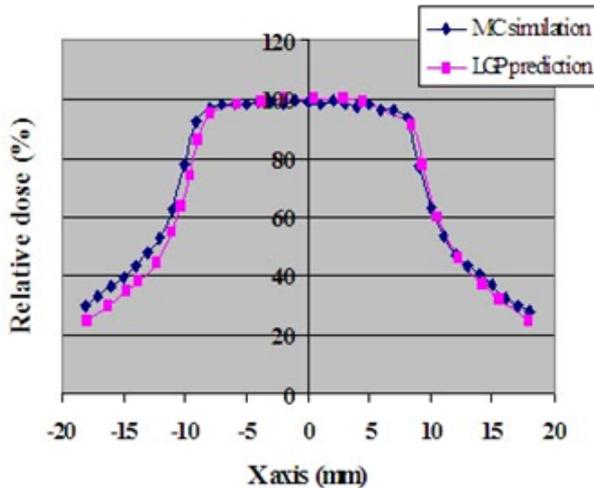


Figure 3. Relative dose profile along X axis obtained using LGP prediction and MC simulation for single shot of 18 mm collimator size.

In figure 4 a-d, the 2D dose distributions on axial plane of homogeneous and

inhomogeneous phantoms in irradiation with 8 mm collimator of GK unit have been plotted. The measured distribution on this plane showed a relative dose to 90%, and spatial uncertainty between isodose lines in homogeneous and inhomogeneous phantoms within ± 2 mm; however, within the relative doses higher than 90%, spatial uncertainty exceeded the acceptance criterion (± 2 mm). The results were also confirmed by calculated isodose lines (4a and 4b).

Figure 5 (a-d) shows the results for 18 mm collimator of GK unit. The results were consistent with those differences which can be observed in figure 4 for 8 mm collimator.

The measured dose difference between maximum relative doses in air was inserted, and PTFE inserted phantoms for both 8 mm and 18 mm collimators exceeded 7%, i.e., in PTFE inserted phantom relative dose at most could have reached 96% and in air inserted phantom it exceeded 104%. The same results were obtained using MC simulation.

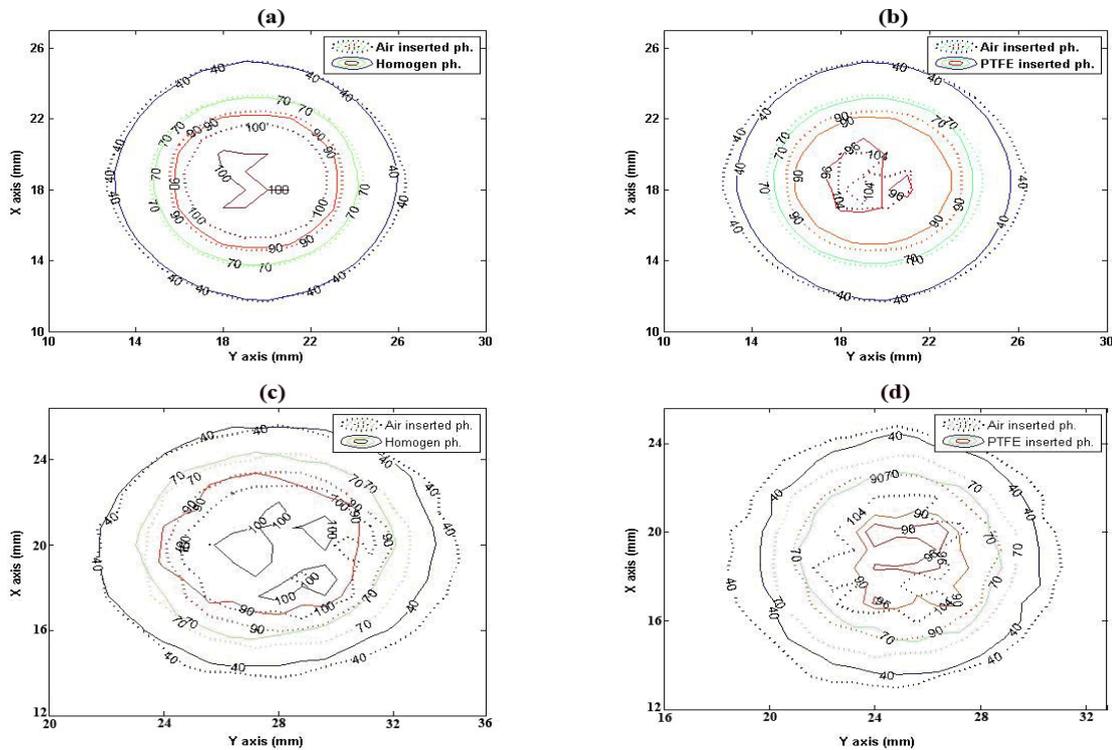


Figure 4. 2D dose distribution in axial plane in irradiation with 8 mm collimator of GK unit obtained using simulation (a and b) and PAGAT Polymer gel dosimeter (c and d). Dashed lines are isodose lines in air inserted phantoms and full lines are isodose lines in homogeneous (a and c) or PTFE inserted phantoms (b and d).

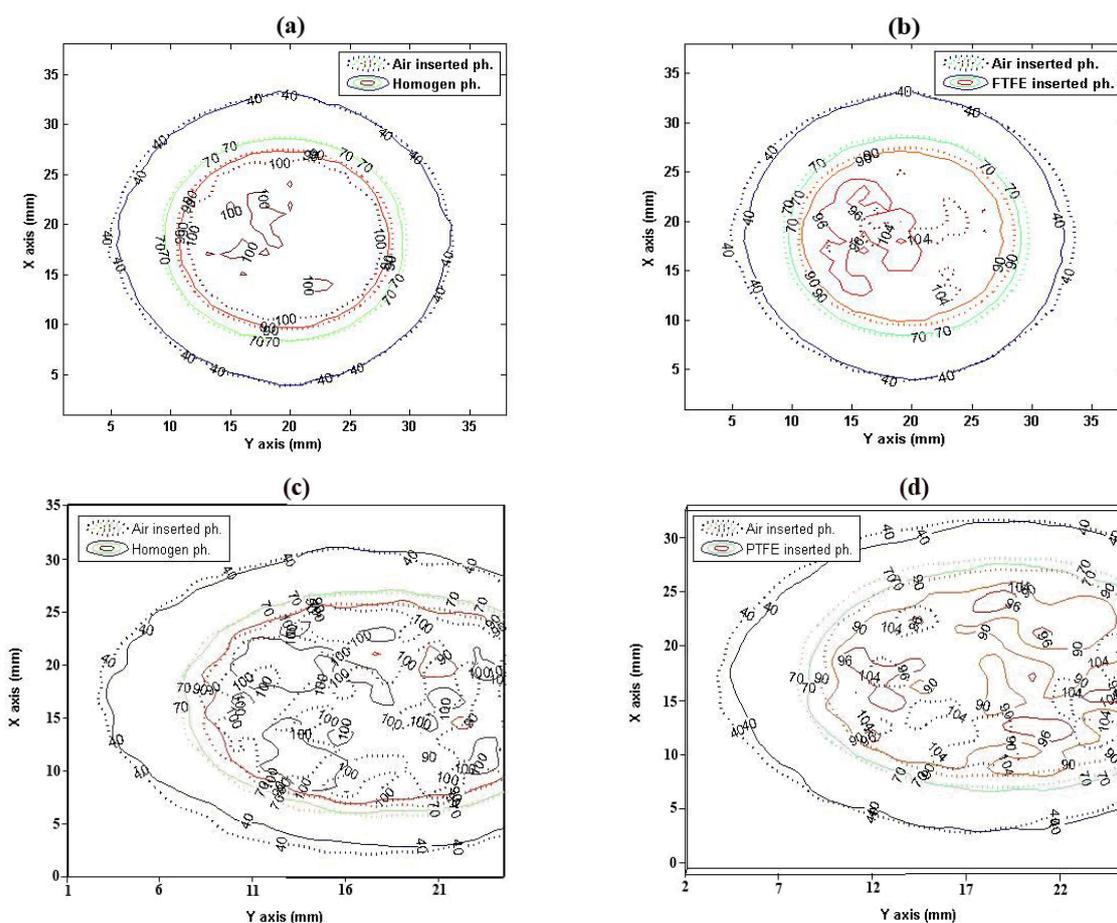


Figure 5. 2D dose distribution in axial plane in irradiation with 18 mm collimator of GK unit obtained using simulation (a and b) and PAGAT Polymer gel dosimeter (c and d). Dashed lines are isodose lines in air inserted phantoms and full lines are isodose lines in homogeneous (a and c) or PTFE inserted phantoms (b and d).

DISCUSSION

The total positioning error, based on the surface contouring accuracy, MRI fiducial correspondence and overall positioning accuracy of the Gamma Knife was ± 2 mm, similar to the error expected for patient treatment⁽¹⁹⁾. The results of simulation and measurement with 8 and 18 mm collimators of GK unit demonstrated that the distance between relative isodose curves exceeded the total positioning error within high isodose levels (i.e., >90%).

Regarding acceptance criteria for conformal radiation therapy, it was important to avoid delivering less than 93% of prescription dose to larger than 1% of the target or more than 110% of the prescription dose to greater than 20% of the target⁽³²⁾.

The results showed that in some

situations (e.g., presence of both air and PTFE within phantom) the mentioned criterion might not be guaranteed, i.e., dose difference exceeded 7%, which meant, less than 93% of prescription dose might be delivered to the target.

Isbakan *et al.*⁽³³⁾ found considerable differences between diameter of isodoses lower than 80% between homogeneous and inhomogeneous phantoms in their study using MAGIC gel dosimeter which is in contrast with the findings of the present research. According to their study, the diameters of the 50% isodose curves differed 43% in the X axis and 32% in the Y axis in homogeneous, and air inserted phantom. Our study showed no considerable differences between lower isodose lines. Maskvin *et al.*⁽¹⁹⁾, using conventional dosimeters and simulation (PENELOPE), found that the

dose delivered to the target area away from an air-tissue interface may be underestimated by up to 7% by GammaPlan due to overestimation of attenuation of photon beams passing through air cavities. Their finding is similar to the one's of this study in air inserted phantom.

Al-Dweri *et al.* ⁽¹⁷⁾ determined dose distribution for heterogeneous phantoms including the bone- and/or air-tissue interfaces showed non-negligible differences with respect to those calculated for a homogeneous one, mainly when the Gamma Knife isocenter approaches the separation surfaces. Their findings confirmed an important underdosage (~10%) nearby the air-tissue interface. However, their study was in interfaces of bone- and/or air-tissue and somewhat different from our goal of study.

CONCLUSION

The observed discrepancies in results of simulation and MRI-polymer gel dosimetry between homogeneous and inhomogeneous phantoms, suggested that LGP predictions must be corrected in order to take care of the air- and bone-tissue inhomogeneities.

In this respect it is worthwhile to mention that an air inhomogeneity that could be assumed as maxillary frontal sinuses gives rise to modifications of the dose distribution which was considerable in some situations.

Moreover, finding of comparative dose profile between LGP and MC simulation confirmed that the applied code is a proper tool for verifying the accuracy of 3D dose distribution in treatment with GK unit.

REFERENCES

- Leksell L (1951) The stereotaxic method and radiosurgery of the brain. *Acta Chir Scand*, **102**: 316-19.
- Mack A, Scheib SG, Major J, Gianolini S, Pazmandi G, Feist *et al.* (2002) Precision dosimetry for narrow photon beams used in radiosurgery-determination of Gamma Knife output factors. *Med Phys*, **29**: 2080-9.
- Fong PM, Keil DC, Does MD, Gore JC (2001) Polymer gels for magnetic resonance imaging of radiation dose distributions at normal room atmosphere. *Phys Med Biol*, **46**: 3105-13.
- Venning AJ, Nitschke K, Keall PJ, Baldock C (2005) Radiological properties of normoxic polymer gel dosimeters. *Med Phys*, **32**: 1047-53.
- DOSGEL (1999) Proc. 1st Int. Workshop on Radiation Therapy Gel Dosimetry (Lexington, KY, USA). ed L J Schreiner and Audet.
- DOSGEL (2001) Proc. 2nd Int. Workshop on Radiation Therapy Gel Dosimetry (Queensland University of Technology, Brisbane, Australia). ed C Baldock and De Deene.
- DOSGEL (2004) Proc. 3rd Int. Workshop on Radiation Therapy Gel Dosimetry (Ghent University, Ghent, Belgium). ed Y De Deene and C Baldock.
- DOSGEL (2006) Proc. 4th Int. Workshop on Radiation Therapy Gel Dosimetry (Sherbrooke University, Sherbrooke, Quebec, Canada). ed M Lepage, A Jirasek, L J Schreiner.
- Ertl A, Saringer W, Heimberger K, Kindl P (1999) Quality assurance for the Leksell gamma unit: considering magnetic resonance image-distortion and delineation failure in the targeting of the internal auditory canal. *Med Phys*, **26**: 166-70.
- Guo WY, Chu WC, Wu MC, Chung WY, Gwan WP, Lee YL *et al.* (1996) An evaluation of the accuracy of magnetic-resonance-guided Gamma Knife surgery. *Stereotact Funct Neurosurg* **66 Suppl**, **1**: 85-92.
- Watanabe Y, Akimitsu T, Hirokawa Y, Mooij RB, Perera GM (2005) Evaluation of dose delivery accuracy of Gamma Knife by polymer gel dosimetry. *J Appl Clin Med Phys*, **6**: 133-42.
- Novotny J, Dvorak P, Spevacek V, Tintera J, Novotny J, Cechak T *et al.* (2002) Quality control of the stereotactic radiosurgery procedure with the polymer-gel dosimetry. *Radiother Oncol*, **63**: 223-30.
- Ertl A, Berg A, Zehetmayer M, Frigo P (2000) High-resolution dose profile studies based on MR imaging with polymer BANG(TM) gels in stereotactic radiation techniques. *Magn Reson Imaging*, **18**:343-9.
- Novotny J, Jr., Novotny J, Spevacek V, Dvorak P, Cechak T, Liscak R *et al.* (2002) Application of polymer gel dosimetry in gamma knife radiosurgery. *J Neurosurg*. **97(5 Suppl)**: Supplement **5**: 556-62.
- Scheib SG and Gianolini S (2002) Three-dimensional dose verification using BANG gel: a clinical example. *J Neurosurg*, **97**: 582-7.
- Cheung JY and Yu KN (2005) "Dose distribution close to metal implants in gamma knife radiosurgery: a Monte Carlo study" [*Med. Phys*, **30**: 1812-1815 (2003)]. *Med Phys*, **32**: 1448-9.
- Al-Dweri FM, Rojas EL, Lallena AM (2005) Effects of bone- and air-tissue inhomogeneities on the dose distributions of the Leksell Gamma Knife calculated with PENELOPE. *Phys Med Biol*, **50**: 5665-78.
- Lewis RD, Ryde SJS, Seaby AW, Hancock DA, Evans CJ (2000) Use of Monte Carlo computation in benchmarking radiotherapy treatment planning system algorithms. *Phys Med Biol*, **45**: 1755-64.
- Moskvin V, Timmerman R, DesRosiers C, Randall M, DesRosiers P, Dittmer P *et al.* (2004) Monte carlo simulation of the Leksell Gamma Knife: II. Effects of heterogeneous versus homogeneous media for

- stereotactic radiosurgery. *Phys Med Biol*, **49**: 4879-95.
20. Allahverdi Pourfallah T, Allahverdi M, Riahi Alam N, Ay MR, Zahmatkesh MH (2009) Differential dose volume histograms of Gamma Knife in the presence of inhomogeneities using MRI-polymer gel dosimetry and MC simulation. *Med Phys*, **36**: 3002-12.
 21. Venning AJ, Hill B, Brindha S, Healy BJ, Baldock C (2005) Investigation of the PAGAT polymer gel dosimeter using magnetic resonance imaging. *Phys Med Biol*, **50**: 3875-88.
 22. De Deene Y, Vergote K, Claeys C, De Wagter C (2006) The fundamental radiation properties of normoxic polymer gel dosimeters: a comparison between a methacrylic acid based gel and acrylamide based gels. *Phys Med Biol*, **51**: 653-73.
 23. MathWorks (2007) Image Processing Toolbox 5. MATLAB v 7.
 24. De Deene Y, Van de Walle R, Achten E, De Wagter C (1998) Mathematical analysis and experimental investigation of noise in quantitative magnetic resonance imaging applied in polymer gel dosimetry. *Signal Processing*, **70**: 85-101.
 25. Pourfallah TA, Allahverdi M, Alam NR, Ay MR, Zahmatkesh MH, Ibbott GS (2009) Performance evaluation of MRI-based PAGAT polymer gel dosimeter in an inhomogeneous phantom using EGSnrc code on a Co-60 machine. *Appl Radiat Isot*, **67**: 186-91.
 26. Kawrakow I, Mainegra-Hing E, Rogers DWO (2004) EGSnrcMP: the multi-platform environment for EGSnrc. NRCC Report PIRS-877.
 27. Rogers DWO, Walters B, Kawrakow I (2007) BEAMnrc Users Manual. NRCC Report PIRS-0509 (A) rev1.
 28. Treurniet JR, Walters BR, Kawrakow I, Rogers DWO (2005) BEAMnrc, DOSXYZnrc and BEAMDP GUI User's Manual. NRCC Report PIRS-0623 (rev C).
 29. Walters B, Kawrakow I, Rogers DWO (2007) DOSXYZnrc Users Manual. NRCC Report PIRS-794 (revB).
 30. Moskvin V, DesRosiers C, Papiez L, Timmerman R, Randall M, DesRosiers P (2002) Monte Carlo simulation of the Leksell Gamma Knife: I. Source modelling and calculations in homogeneous media. *Phys Med Biol*, **47**: 1995-2011.
 31. Al-Dweri FM, Lallena AM, Vilches M (2004) A simplified model of the source channel of the Leksell GammaKnife tested with PENELope. *Phys Med Biol*, **49**: 2687-703.
 32. Perez CA, Brady LW, Halperin EC, Schmidt-Ullrich RK (2004) Principles and Practice of Radiation Oncology. LIPPINCOTT WILLIAMS & WILKINS, Philadelphia, USA. 4th ed: 968.
 33. Isbakan F, Yekta Ülgen Y, Bilge H, Ozen Z, Agus O, Büyüksarac B (2007) Gamma Knife 3-D dose distribution near the area of tissue inhomogeneities by normoxic gel dosimetry. *Medical Physics*, **34**: 1623-30.