Electron Paramagnetic Resonance Spectroscopy for Gamma Knife Dosimetry

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Abstract. Alanine chips exposed to high doses of radiation produces long lived free radicals that could be easily measured with electron paramagnetic resonance (EPR) spectrometers. In this study, the feasibility of using alanine dosimeters for performing rapid quality assurance of Leksell Gamma Knife (LGK) treatment plans was demonstrated. A 3D printed grid was placed inside the LGK spherical solid water phantom (SWP) for measurement of doses at isocentre and off-axis points. The EPR spectroscopy was performed on a Magnettech MS-5000 EPR/ESR spectrometer. A set of dose calibration curves were established prior to the use of alanine chips for LGK dosimetry. Absolute dose, transit dose and dose/timer linearity were performed with the alanine chips positioned at the centre of the LGK solid water phantom (SWP). Five patients of different sites were selected, and patient specific quality assurance (PSQA) was performed in the LGK SWP. The absolute dose measured with the EPR alanine dosimeter agreed well within 2% of the ion chamber results and PSQA results were within 2.1%. Alanine-based EPR dosimetry offers rapid dose measurement with high accuracy and can also be used as a dosimeter for Gamma Knife PSQA.

1. Introduction
Electron Paramagnetic Resonance (EPR) was discovered by Yevgeny Zavoisky in 1944 [1] and predates the discovery of the more familiar Nuclear Magnetic Resonance (NMR) and Magnetic Resonance Imaging (MRI). EPR shares the same basic physics as NMR with the difference that it involves the magnetic moment from unpaired electrons rather than nuclear spin from protons and neutrons. The energy of a free electron in a magnetic field is described by the Electron Zeeman splitting.

$$\textbf{H} = g_e \beta_e \textbf{S} \cdot \textbf{B}$$ (1)

If we assume the magnetic field is in the $z$ direction, then

$$\textbf{H} = g_e \beta_e S_z B$$ (2)

$$S_z = \begin{bmatrix} 1 \frac{1}{2} & 0 \\ 0 & -\frac{1}{2} \end{bmatrix}$$ (3)

$$E = \pm \frac{1}{2} g_e \beta_e B$$ (4)
As in NMR, resonant absorption occurs when the energy of the applied electromagnetic radiation is equal to the Zeeman splitting between the two spin states. The Bohr Magneton ($\beta_e$) is approximately 1836 times greater than the Nuclear Magneton and at typical magnetic fields of approximately 0.35 T this yields a resonant frequency of 10 GHz which is in the microwave region [2]. The microwave source in an EPR spectrometer is a Klystron or in modern instruments a solid-state Gunn diode. Magnets are typically an electromagnet rather than a superconducting magnet and, in most spectrometers, the magnetic field is swept rather than the frequency. Magnetic field modulation and phase sensitive detection is also used to improve sensitivity resulting in a derivative line shape.

![Figure 1. Electron Zeeman splitting and resonant absorption.](image)

In contrast to NMR where hydrogen nuclei with unpaired nuclear spins are ubiquitous in the human body most electrons in human tissue are paired in bonds and have no net spin. Highly reactive chemical species with unpaired electrons, called free radicals, are produced in the human body during radiotherapy but have concentrations to low and lifetimes too short to be measured directly by EPR. Long lived free radicals may be produced in certain materials and provide a method for directly measuring the absorbed dose in a sample. The amplitude of the EPR signal is directly proportional to the number of free radicals which is in turn proportional to the absorbed dose. EPR is the only technique that directly detects free radicals.

In the 1960s, the alanine/electron paramagnetic resonance (EPR) system was proposed as a tool for radiation dosimetry [3]. Alanine has a long-lived stable free radical, has good tissue equivalence, is non-toxic, has a linear dose response over a large range (1 Gy to 100 kGy), and is energy independent over a wide range of energies. Like thermoluminescent dosimetry (TLD) and optically stimulated luminescence dosimetry (OSLD), EPR dosimetry does not give an immediate result and requires a specialized spectrometer for readout. EPR has the advantage that the readout does not erase the dosimeter and they can be reread indefinitely with no signal loss. Early research indicated that more than one species of radical was formed during irradiation each giving rise to a slightly different EPR spectrum [4, 5]. The drawbacks of alanine are as follows: (i) dose uncertainty below 1 Gy, multiple radicals in different proportions produce complicated spectrum and it is also sensitive to humidity and water.

The Leksell Gamma Knife (LGK) Perfexion (PFX), a dedicated intracranial-based external beam radiotherapy unit contains 192 $^{60}$Co sources focussed at the isocentre. Unlike the previous gamma knife units, the PFX system contains eight position controlled movable sectors of 24 sources each to produce shot sizes of 4, 8 and 16 mm and eliminates the time taken to manually set up the collimator position for multiple treatment shots. In this study, an effort has been made to explore the feasibility of using a bench top EPR spectrometer for Gamma Knife radiotherapy.

2. Methods

The alanine dosimeters are read using the Magnettech MS-5000 (Freiburg instruments, Germany), a bench-top dosimeter (Figure 2) recently acquired at the Princess Alexandra Hospital. The MS-5000 EPR spectrometer has a magnetic field range of 30 to 650 mT with a field resolution of 0.03 µT. The
MS-5000 has two dose ranges to read doses from 0.5 kGy to >200 kGy (High dose: 10s acquisition time, 8000 readouts/day) and <1 to 20 Gy (Low dose mode: 120s acquisition time).

Figure 3 illustrates the increase in the peak-to-peak value with the increase in the delivered dose. A 3D printed alanine grid insert was designed to house the EPR alanine chips (Figure 4a). The grid was placed inside the LGK spherical solid water phantom for dose measurement at isocentre and off-axis points (Figure 4b). A set of dose calibration curves were established by exposing the alanine chips placed inside the SWP to doses ranging from 0.5 Gy to 50 Gy. Absolute dose, transit dose and dose/timer linearity were performed with the alanine chips positioned at the centre of the LGK solid water phantom (SWP). Five treatment plans generated for different treatment sites (haemangioblastoma, pituitary adenoma, brain metastasis, recurrent glioblastoma and vestibular schwannoma) were selected, and treatment plans were exported onto the SWP. The dose calculated for the above plans were compared against the alanine measured dose in the SWP.

3. Results and Discussion

The absolute dose measured with the EPR alanine dosimeter agreed well within 2% of the ion chamber results. Alanine-based EPR dosimetry offers rapid dose measurement with high accuracy can also be used as a potential dosimeter for PSQA. Figure 5 shows the 40 Gy (Gamma Plan prescribed dose) EPR signal measured at the isocentre for a 16 mm shot.
Figure 6 demonstrates the results of timer linearity/transit dose measured using CC13 (a) and the alanine EPR dosimeter (b). Table 1 highlights the results of the measured and Gamma Plan computed dose for all five sites. For most patients, the agreement between the measurement and calculated dose was within 2%. Alanine’s near tissue equivalence, high precision and low energy dependence makes it one of the highly preferred dosimeters in radiotherapy. The Magnettech MS-5000 EPR reader provides an easy and quick turn-around time for alanine-based dosimetry in radiotherapy.

Table 1. Comparison of measured (alanine) vs Gamma Plan computed dose.

| Case No. | 1     | 2     | 3     | 4     | 5     |
|---------|-------|-------|-------|-------|-------|
| Diagnosis | Hemangioma | Pituitary Adenoma | Brain metastasis | Glioblastoma | Vestibular Schwannoma |
| MR axial slice | ![Image](image1.png) | ![Image](image2.png) | ![Image](image3.png) | ![Image](image4.png) | ![Image](image5.png) |
| TPS calculated dose (Gy) | 9.00 | 7.50 | 16.20 | 19.10 | 15.90 |
| EPR measured dose (Gy) | 9.15 | 7.66 | 16.21 | 18.93 | 15.60 |
| Difference (%) | 1.7 | 2.1 | 0.6 | 0.9 | 1.9 |

4. Conclusions

The absolute dose measured with the EPR alanine dosimeter agreed well within 2% of the ion chamber results. Alanine-based EPR dosimetry shows promising and comparable results in Gamma Knife dosimetry and can be used as a dosimeter for patient specific quality assurance suited well for Gamma Knife plans (8 Gy – 180 Gy).

5. References

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