Preliminary investigation of PAGAT polymer gel radionuclide dosimetry of Tc-99m

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Abstract PAGAT polymer gel was investigated as a suitable dosimeter materials for measuring absorbed dose from the unsealed source radionuclide Tc-99m. Differing amounts of Tc-99m over the range of 25-5000 MBq were introduced into a normoxic polymer gel mixture (PAGAT) in sealed nitrogen-filled P6 glass vials. After irradiation the gels were evaluated using MRI more than 48 hours after preparation to allow for radioactive decay. The dose delivered to the vial was also calculated empirically. R2 versus total activity curves were obtained over a number of experiments and these were used to evaluate the relationship between the amount of gel polymerization and the dose deposited by the radionuclide. A linear response up to 1000 MBq (corresponding to 20Gy) was displayed and was still behaving monotonically at 5000 MBq. Polymer gels offer the potential to measure radiation dose three-dimensionally using MRI.

1. Introduction
Treatments involving the use of ionizing radiation such as radiotherapy and targeted radionuclide therapy play an essential role in medicine and are becoming ever more commonplace with the development of new therapies and technologies. With these treatments comes the need for dosimetry in order to measure the amount of absorbed radiation dose to ensure patient health and safety and to reduce the health risks that can result from an overexposure to radiation. Dosimetry is important both for having the ability to reproduce and compare treatments and techniques and for knowing the limit beyond which administered radiation would cause harmful side effects. A variety of dosimetry techniques exist which can provide precise absorbed dose measurements in one or two dimensions. However, while one and two dimensional dosimeters can provide accurate and precise dose measurements, they have limitations such as in the dosimetry of high dose gradients or in the ability to provide adequate spatial resolution in three dimensions. Polymer gel dosimetry however can provide true three-dimensional absorbed dose information [1,2,3,4].

Gel dosimeters have primarily been studied in the context of clinical radiotherapy in order to evaluate dose distributions from external radiation beams. The most common gel formulations are known as polymer gels, which consist of monomers that polymerize upon irradiation. These dosimeters can be employed to verify absorbed dose estimates from treatment planning systems and to analyze dose gradients created by multileaf collimator systems. Polymer gel dosimeters have the potential to increase the accuracy of radiotherapy treatments and to aid in the development of more personalized dosimetry for treatment plans [1,2,3,4].
In nuclear medicine, radiopharmaceuticals, pharmaceuticals tagged with radioactive isotopes, are administered to the patient orally, intravenously, or through inhalation. The radiopharmaceutical partakes in a certain physiological pathway and is taken up by the organ of interest. Once it is administered, the radionuclide causes photons and/or charged particles to be emitted within the body. Gamma cameras, SPECT or PET cameras are used in order to detect the emergent photons. For diagnostic imaging, only trace amounts of radiopharmaceuticals are administered. In targeted radionuclide therapy, higher doses of radiopharmaceuticals are used in order to treat and eradicate tumours. Dosimetry for radionuclide therapy and diagnostic studies currently relies on imaging in order to map the distribution of the radiopharmaceutical in the body. The images obtained are quantified in order to measure the activity of the radiopharmaceutical in a certain part of the body at a given time in which corrections must be applied in order to finally calculate the absorbed dose distribution.

There is a clear need for a standardized method of radionuclide absorbed dose calculations. Dosimetry in nuclear medicine may be performed in different ways by different clinics or may not be performed at all because of the time required for such calculations and the potentially large uncertainties associated with the calculated doses. The lack of standardized methodology thus means that treatments delivered in different clinics may not be consistent. While accurate absorbed dose calculations have been developed for radiotherapy and have been adopted worldwide, radionuclide absorbed dose calculations used clinically are still approximations at best. The integration of polymer gel dosimeters into nuclear medicine radionuclide dosimetry will potentially provide an accurate method of calculating absorbed dose and aid in the standardization of dose calculation methods. This is coupled with the recent introduction of combined multi-modality SPECT/CT and PET/CT scanners thus providing anatomical electron density maps (the CT scan) and the distribution of the radiopharmaceutical, affording new possibilities for determining individualised dose plans for internal radionuclide therapy.

Absorbed radiation dose from radionuclides are more difficult to measure than the dose from an external beam of radiation. Current absorbed dose measurements in radiotherapy measure the absorbed dose to water from a beam of radiation and use correction factors to account for inconsistencies and inhomogeneities associated with the measurement. Doses are measured over the period during which the radiation beam is turned on. Conversely, absorbed dose measurements in nuclear medicine must take into account the fact that the radionuclide is located within the body and causes a decaying absorbed dose to accumulate. Measurements must therefore be taken over the entire period of time in which the radionuclide is active within the body. Depending on the physical and biological half-lives of the radionuclide, the absorbed dose will be deposited over a period of hours or days.

Promising results from polymer gel radiotherapy studies sparked an interest in investigating the use of gel dosimeters for internal dosimetry in nuclear medicine [5,6,7]. The previous radionuclide dosimetry studies using gel dosimetry for radionuclide therapy used MRI to evaluate the radionuclide dose deposited in a MAGIC polymer gel dosimeters [8]. The studies found a relationship between dose and the amount of polymerization, indicated by change in R2.

The current study aimed to investigate the dosimetry of Technetium-99m (Tc-99m) in conjunction with the PAGAT normoxic polymer gel dosimeter [9] for the purposes of diagnostic nuclear medicine dosimetry. The radiation dose from different activities of the radionuclide was measured by analyzing the radiation-induced change in the gels with MRI.

2. Materials and Methods
The formulation used for the PAGAT gel was according to Venning et al. [9]. The gelatin was added to deionized water and allowed to soak for fifteen minutes. The solution was then heated to 50°C and stirred with a magnetic stir bar in order for the gelatin to dissolve in the water. Once the temperature of the solution had reached 50°C, the temperature was held constant. The gel solution was continuously stirred by the stir bar throughout the course of the experiment in order to thoroughly mix the other
ingredients into the gel. When the solution became clear in colour, indicating that the gelatin had dissolved, the acrylamide was added. The bis-acrylamide was then added once the acrylamide had mixed into the gel, followed by the hydroquinone. The solution was left to stir for five minutes, during which time activities of Tc-99m were added to P-6 nitrogen-filled vials [10,11] via a syringe in up to 5000 MBq. Tetrakis was then added to the gel and stirred for a further two minutes before the gel was added to the Tc-99m in the vials via a syringe. When the gel was added to each vial, the tip of the syringe needle was pushed into the Tc-99m solution to help ensure that the Tc-99m would mix evenly into the gel. After removing the empty syringes, the vial was shaken and stored behind a lead shield. As each of the needles became contaminated with Tc-99m, the needle was replaced before adding gel to other vials in order to avoid contaminating samples with activity from other samples.

The irradiated vials were analyzed within 48 hours post-irradiation using a Siemens Vision 1.5T clinical MRI scanner using the same imaging protocol as used by Venning et al. [9]. T2 weighted imaging was performed using a multiple spin-echo pulse sequence. 64 equidistant spin-echoes were used along with a TE of 20ms and a TR of 5000ms. For this preliminary study, the vials were imaged using two 5mm slices. The first slice was close to the bottom of the vial and therefore might suffer from overlap with the glass. The second slice was closer to the top of the gel and further from the base of the vial. A region of interest was drawn inside the gel in order to avoid inconsistencies in the data from the effects of the glass edges of the vial. The values obtained for each sample were the mean R2 and the associated standard deviation.

Medical Internal Radiation Dose (MIRD) calculations [12,13,14,15] were undertaken to determine the accumulated dose from the Tc-99m to the polymer gel.

3. Results

![Figure 1 R2 plotted against activity.](image)
3. Discussion

This preliminary study has shown that gel dosimeters have the potential for measuring the absorbed dose from Tc-99m radionuclide. Not only do the gels respond to Tc-99m, but they polymerize as a function of the activity of the added radionuclide. PAGAT gels would be potentially good dosimeters for use in nuclear medicine. The gels are not prone to diffusion and therefore the results are a permanent record of the integrated radionuclide dose. PAGAT polymer gels are radiological tissue equivalent.

Several improvements can be made in order to facilitate future experiments. Higher activities such as 7000MBq and 9000MBq should be used in order to provide a better idea of the curve characteristics and the activity at which the gel saturates. More work could be done to determine which syringe size is best for adding gel to the vials or cuvettes in order to ensure the reproducibility of the experiment and the accuracy of the added gel volume. More gel should be added to the P-6 vials in future experiments in order to facilitate MRI analysis. The gel was only divided up into two MRI slices because of the short depth of the gel in the vial. The first slice was close to the bottom of the vial and therefore might suffer from overlap with the glass. Adding more gel would allow for more MRI slices to be taken and thus provide a more accurate analysis of gel polymerization. If more gel is added to the vial, however, more of the radionuclide must also be added.

Future studies will be translated to the use of gels in three-dimensional anthropomorphic phantoms to more closely relate the administered activity to the absorbed dose in the body. The implications of the implementation of gels into nuclear medicine include determining breast dose from sentinel lymph node injections, local dose and the dose to surrounding tissues from radionuclide therapy treatments, or dose from other treatments such as radiation synovectomy.

The use of polymer gel dosimeters to measure the absorbed dose from Tc-99m in diagnostic nuclear medicine has not previously been investigated and is a new method of calculating the absorbed dose from the radionuclide over the length of time that the radionuclide remains active within the patient. This new methodology provides the potential to further personalize treatments and to more accurately calculate dose and future work will examine its utility with other radionuclides.
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