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Internal radiation dosimetry of orally administered radiotracers for the assessment of gastrointestinal motility

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HIGHLIGHTS

- Internal radiation dose estimates for radionuclide GI transit were calculated.
- The ICRP 30 GI tract model, MIRDOSE 3.1 & OLINDA/EXM 1.0 software applications were used.
- The calculated equivalent dose and effective dose for organs were reported.
- The radiation doses among ^{153}Sm, ^{111}In and ^{99m}Tc formulations were compared.
- The calculated doses were in good agreement with the ARSAC published values.

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ABSTRACT

Radionuclide imaging using ^{111}In, ^{99m}Tc and ^{153}Sm is commonly undertaken for the clinical investigation of gastric emptying, intestinal motility and whole gut transit. However the documented evidence concerning internal radiation dosimetry for such studies is not readily available. This communication documents the internal radiation dosimetry for whole gastrointestinal transit studies using ^{111}In, ^{99m}Tc and ^{153}Sm labeled formulations. The findings were compared to the diagnostic reference levels recommended by the United Kingdom Administration of Radioactive Substances Advisory Committee, for gastrointestinal transit studies.

1. Introduction

It is essential that any medical radiation exposure is justified and optimized before use. With increased public awareness of ionizing radiation effects, all imaging studies involving radiation must have commensurate risk and benefit assessments. It is therefore important to estimate the radiation dose received by a patient administered with any amount of a radiopharmaceutical.

Nuclear medicine investigations are regarded as the gold standard for the assessment of gastric emptying and gastrointestinal (GI) motility. A number of potential radionuclides can be used for this purpose, each with advantages and disadvantages of photon energy, physical half-life and radiation dosimetry. The main radionuclides that have been employed are Indium-111 (^{111}In) and Technetium-99m (^{99m}Tc) which are incorporated into non-absorbable forms for oral administration. An alternative radionuclide, Samarium-153 (^{153}Sm) in the form of resin-based formulation, has recently been developed and tested to assess whole gut motility in constipated patients (Yeong, et al., 2011, 2012). The advantages of ^{153}Sm include minimal radiation exposure to radiopharmacy staff, improved manufacturing and radioactive transportation, workflow and potentially

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wider global availability through local production using a research reactor, hence resulting in lower cost. There are currently 246 research reactors in operation worldwide according to the IAEA research reactor databases (International Atomic Energy Agency, 2014). Nevertheless, there is a lack of published information on the effective dose resulting from the oral administration of ^{153}Sm. Current literature states that for ^{153}Sm (used in scintigraphic studies of drug delivery), an oral ingestion of 1 MBq of ^{153}Sm delivers an effective dose of 0.7 mSv (Ahrabi et al., 1999a, 1999b, 2000; Awang et al., 1993; Fani et al., 2002; Marvola et al., 2004, 2008). However the basis for this estimation is untraceable.

Unlike radiation doses received from external sources such as medical imaging X-ray devices, internal dose cannot be directly measured. Doses from radiopharmaceuticals are normally calculated from standardized models, assumptions and procedures (Stabin, 1996). In general, the calculation of internal dose has been performed by summing the radiation absorbed in various target tissue, from a number of source organs that contain significant quantities of the radionuclide. In nuclear medicine, the most commonly used method for the calculation of internal dose estimates is that developed by the Medical Internal Radiation Dose (MIRD) Committee of the Society of Nuclear Medicine and Molecular Imaging (SNMMI), United States (Toohey et al., 2000). The MIRD schema uses a unique set of symbols and quantities to calculate the absorbed dose in specified target organs from radioactive decays that occur in source organs.

This communication describes the estimation of the radiation dose including target organ equivalent dose (H_T) and effective dose (E) from the orally ingested radionuclides, i.e. ^{99m}Tc, ^{111}In and ^{153}Sm used for GI transit scintigraphy, to provide clinicians and researchers the relative risks associated with in vivo clinical studies.

2. Materials and methods

The H_T and E for ^{99m}Tc, ^{111}In and ^{153}Sm were calculated using the MIRDOSE 3.1 and OLINDA/EXM 1.0 software (Vanderbilt University, Nashville, Tennessee, United States). The pharmacokinetic data were incorporated into the ICRP 30 GI tract model. The mathematical model and software which gave the best fitted results to the published dosimetry data for ^{111}In and ^{99m}Tc were then used to extrapolate the radiation dose for ^{153}Sm-labeled resin formulations.

2.1. MIRDOSE 3.1

MIRDOSE 3.1 internal radiation dose assessment software was obtained from the Oak Ridge Associated Universities, Tennessee, United States. This program performs internal radiation dose calculations using the medical internal radiation dosimetry (MIRD) method (Toohey et al., 2000).

The system computes the absorbed dose to each target organ and total body (expressed in mGy MBq^{-1} and rad mCi^{-1}), effective dose equivalent (H_T) and effective dose (E) per unit of administered activity (expressed in mSv MBq^{-1} and rem mCi^{-1}). The percentages of primary and secondary source organ that contributed to the target organ dose were also included.

The "Adult (70 kg)" mathematical phantom was chosen which represented a male adult with a standard size of 70 kg. For female adults, the choices of models provided were non-pregnant, 3-month, 6-month and 9-month pregnant. Only the "Adult Female – Non-pregnant" model was used in this study. The ICRP 30 GI tract model was used to obtain the residence time and kinetic data. Given a fraction of activity entering the stomach at time zero and knowledge of how much is absorbed from the small intestine, the cumulated activities in all segments can be calculated. In this study, labeled non-absorbable compounds (ion-exchange resin) were studied, and the assumption was made that the fraction of activity entering stomach was 1.0 and the fraction of activity absorbed from the small intestine was zero. Table 1 shows the parameters used in the GI tract model.

H_T and E were then calculated using the software. The equivalent dose attributed to different types of radiation (β, γ- and X-ray) was also calculated. Using the same phantom and kinetic model, the radiation dose given by the same formulation but labeled with different radionuclides, ^{111}In and ^{99m}Tc were calculated and the data were compared with ^{153}Sm.

2.2. OLINDA/EXM 1.0

OLINDA/EXM 1.0 internal radiation dose assessment software was used to calculate H_T and E for the administered formulation. As was the case for MIRDOSE 3.1, the internal radiation dose assessment was based on the mathematical formulism developed by the MIRD Committee of the SNMMI, United States (Loevinger et al., 1988). While MIRDOSE 3.1 was written in Microsoft's Visual Basic language and run under the Windows operating system, the OLINDA/EXM 1.0 was written in Java programming language. Similar to the methods in MIRDOSE 3.1, the internal radiation doses were calculated and compared.

2.3. ICRP 30 GI tract model

The mathematical model of the GI tract was developed based on the ICRP 30 GI model data (ICRP, 1979a, 1979b). The model describes the GI tract as a four compartmental model with first order, one-way flow between compartments, and one pathway to the blood stream from the small intestine, as shown in Fig. 1.

Table 1
Summary of parameters used in the mathematical model of the GI tract.

Model	**GI tract model, adult male and female**					
Route of entry	Oral consumption, passing through					
Fraction of activity absorbed	Fraction of activity enters stomach: 1.0 Fraction of activity absorbed by stomach: 0.0 Fraction of activity enters small intestine: 1.0					
Residence time (Bq h Bq^{-1})	**Male**			**Female**		
	^{153}Sm	**^{111}In**	**^{99m}Tc**	**^{153}Sm**	**^{111}In**	**^{99m}Tc**
Stomach contents	10.90	0.99	0.90	0.99	0.99	0.90
Small intestines contents	3.80	3.80	2.45	3.72	3.80	2.45
Upper large intestines contents	10.90	10.90	3.19	10.10	10.90	3.19
Lower large intestines contents	16.10	16.10	1.56	13.80	16.10	1.56