PROPOSED REVISION TO THE RADIATION DOSIMETRY OF ^{82}RB

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Abstract—**Three models for the biodistribution and dosimetry of ^{82}Rb-chloride were reviewed and a proposal is made for the best dosimetry for this agent to be adopted. Data from three proposed biokinetic models for ^{82}Rb-chloride were used to calculate dose estimates for the compound, and the results were compared. The blood content-based model was found to produce dose estimates that were considered to be overly conservative, and a blood flow-based model, which showed good agreement with available measured data, was considered to be more reasonable. A new set of dose estimates for ^{82}Rb-chloride, based on the blood flow-based kinetic model are suggested for general use.**

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Key words: dose, internal; dosimetry; medical radiation; nuclear medicine

INTRODUCTION

As noted in a recent review of dosimetry for agents used in nuclear cardiology (Stabin 2008a), two established models for the dosimetry of the short-lived tracer ^{82}Rb-chloride provide estimates of effective dose that are different by more than a factor of 4. The estimates of the International Commission on Radiological Protection (ICRP 1988) are more conservative, suggesting a value of 0.0034 mSv MBq^{-1} for the effective dose. Another model, based on data collected in human subjects by Ryan et al. (1985), suggested a value of 0.00079 mSv MBq^{-1}. Ryan et al. collected data in two human subjects over about 10 min post injection, using an Anger camera configured to image the 511 keV photons. The review article (Stabin 2008a) recommended use of the more conservative ICRP model, which relied on theoretical assumptions of blood content in different organs of the body. Due to the significant differences in these models, and a perception that use of the more conservative ICRP model was causing an overestimate of dose and risk and a subsequent unnecessary reduction in the amount of activity permitted to be given to patients, an attempt was made here to review the assumptions and results of these models and evaluate which model is most reasonable to use in routine practice. During this study, an article by Leggett et al. (1996) was also reviewed. Leggett et al. proposed a new model for blood circulation and specifically addressed how implementation of this new model would affect time-activity integrals assigned to different tissues and estimates of absorbed dose for ^{82}Rb (as well as for ^{11}CO). Assigning disintegrations to organs based on blood *flow* rather than blood *content* was proposed for nuclides whose physical half-times are short compared to the time required for activity in blood to become reasonably uniformly distributed in an organ. This resulted in differences in assigned cumulated activities in many organs compared to those predicted by a model based on blood content. All three models and their resulting dose estimates for this compound will be reviewed and a proposal will be made for the most appropriate model for this agent to be used.

MATERIALS AND METHODS

The organ cumulated activities [designated as numbers of disintegrations in source organs in the RAdiation Dose Assessment Resource (RADAR) dose assessment system (Stabin and Siegel 2003)] for all three models were entered in to the OLINDA/EXM (Organ Level INternal Dose Assessment/EXponential Modeling) dose calculational code (Stabin et al. 2005). The ICRP model values were entered directly; those of Leggett et al. were calculated from their stated ratios of cumulated activities between their model and the ICRP model. Absorbed doses for all organs and effective doses were calculated for the reference adult male model. All injected ^{82}Rb was assumed to decay in the body; the total number of disintegrations possible is 0.03133 MBq-h per MBq administered. Disintegrations not assigned to individual organs were apportioned to all other tissues in proportion to their mass. As ^{82}Rb activity is assumed to be in the walls of hollow organs due to blood flow rather than in the contents as excreted activity, an adjustment must be made to the doses given by standard

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software programs that assign activity in the hollow organs, as the dose factors for electrons are based on the idea of organ contents irradiating the organ wall (Stabin 2008b). Specifically, the absorbed fraction:

$$\Phi(wall \leftarrow contents)_{\text{electrons}} = \frac{1}{2 \times m_{\text{contents}}}$$

was changed to:

$$\Phi(wall \leftarrow wall)_{\text{electrons}} = \frac{1}{m_{\text{wall}}}.$$

This adjustment was applied to the doses for the stomach and small and large intestines.

RESULTS

The numbers of disintegrations in major source organs for the three models are shown in Table 1. Ratios of the values for the ICRP and Ryan et al. models to those of Leggett et al. are shown in Table 2. In all cases except liver, the ICRP model predicts significantly more disintegrations in the major organs than the Leggett et al. flow-based model. However, the results of the Leggett et al. flow-based model are in quite good agreement with the available measured values of Ryan et al., the greatest difference being with heart wall (27%), and others within ~5–15%. Dose estimates provided by the OLINDA/EXM software for all three models are shown in Table 3.

DISCUSSION

The model based on the Ryan et al. data was intuitively appealing, as it was based on measured data in human subjects rather than solely upon model assumptions. However, the number of subjects was small, the study was done in the mid-1980's with imaging equipment that was not specifically designed to image positron emitters, sampling over the very short times available was problematic, and activity was quantified in a small number of organs. However, when one compares the measured values with the flow-based model predictions of the Leggett et al. model, the agreement is quite good. Differences between the blood flow-based and blood content-based models of Leggett et al. and the ICRP are most striking for adrenals, kidney, cortical bone, and thyroid. Doses for many other

Table 1. Cumulated activities (MBq h^{-1} MBq administered) in various source organs or tissues in the models.

Source region	ICRP	Leggett et al.	Ryan et al.
Adrenals	3.44×10^{-4}	5.56×10^{-5}	
Cortical bone	1.14×10^{-3}	1.47×10^{-4}	
Trabecular bone	2.86×10^{-4}	2.20×10^{-4}	
Heart wall	1.14×10^{-3}	7.15×10^{-4}	5.25×10^{-4}
Kidneys	6.58×10^{-3}	3.29×10^{-3}	3.11×10^{-3}
Liver	1.66×10^{-3}	1.84×10^{-3}	1.54×10^{-3}
Lungs	2.78×10^{-3}	2.14×10^{-3}	1.95×10^{-3}
Muscle	4.67×10^{-3}	4.67×10^{-3}	
Pancreas	4.86×10^{-4}	3.04×10^{-4}	
Marrow	1.43×10^{-3}	7.15×10^{-4}	
Spleen	1.00×10^{-3}	9.09×10^{-4}	
Thyroid	9.17×10^{-4}	2.41×10^{-4}	
Stomach	6.58×10^{-4}	3.13×10^{-4}	
SI	2.83×10^{-3}	2.83×10^{-3}	
ULI	9.17×10^{-4}	6.55×10^{-4}	
LLI	7.17×10^{-4}	5.12×10^{-4}	
Remainder	3.77×10^{-3}	1.18×10^{-2}	2.24×10^{-2}

Table 2. Ratios of cumulated activities in various organs or tissues between the models of Leggett et al. and ICRP and Ryan et al.

Organ or tissue	ICRP/ Leggett et al.	Ryan et al./ Leggett et al.
Adrenals	6.2	—
Cortical bone	7.8	—
Trabecular bone	1.3	—
Red marrow	2.0	—
Heart wall	1.6	0.73
Kidneys	2.0	0.94
Liver	0.9	0.84
Lungs, pulmonary	1.3	0.91
Lungs, bronchial	0.2	—
Pancreas	1.6	—
Skeletal muscle	1.0	—
Spleen	1.1	—
Stomach and esophagus	2.1	—
Small intestine	1.0	—
Large intestine	1.4	—
Thyroid	3.8	—

Table 3. Radiation doses (mSv/MBq administered) in various target organs or tissues in the models.

Target organ	ICRP	Leggett et al.	Ryan et al.
Adrenals	1.63×10^{-2}	2.81×10^{-3}	4.56×10^{-4}
Bladder	1.21×10^{-4}	2.38×10^{-4}	3.73×10^{-4}
Bone surfaces	7.00×10^{-4}	4.93×10^{-4}	4.76×10^{-4}
Brain	7.64×10^{-5}	1.89×10^{-4}	3.35×10^{-4}
Breast	1.09×10^{-4}	2.07×10^{-4}	3.48×10^{-4}
Gall bladder	2.75×10^{-4}	3.41×10^{-4}	4.34×10^{-4}
Stomach	3.64×10^{-3}	1.92×10^{-3}	6.97×10^{-4}
SI	3.36×10^{-3}	3.45×10^{-3}	4.16×10^{-4}
Upper large intestine	3.68×10^{-3}	2.80×10^{-3}	5.39×10^{-4}
Lower large intestine	3.66×10^{-3}	2.76×10^{-3}	4.70×10^{-4}
Heart wall	3.21×10^{-3}	2.05×10^{-3}	2.01×10^{-3}
Kidneys	1.85×10^{-2}	9.32×10^{-3}	8.85×10^{-3}
Liver	9.31×10^{-4}	9.89×10^{-4}	8.37×10^{-4}
Lungs	2.45×10^{-3}	1.90×10^{-3}	1.75×10^{-3}
Muscles	2.29×10^{-4}	2.30×10^{-4}	3.63×10^{-4}
Ovaries	2.24×10^{-4}	3.21×10^{-4}	3.85×10^{-4}
Pancreas	4.44×10^{-3}	2.81×10^{-3}	4.41×10^{-4}
Red marrow	6.87×10^{-4}	4.86×10^{-4}	3.00×10^{-4}
Skin	9.06×10^{-5}	1.85×10^{-4}	3.29×10^{-4}
Spleen	4.78×10^{-3}	4.30×10^{-3}	4.29×10^{-4}
Testes	8.29×10^{-5}	1.96×10^{-4}	3.47×10^{-4}
Thymus	1.38×10^{-4}	2.31×10^{-4}	3.85×10^{-4}
Thyroid	3.43×10^{-2}	9.07×10^{-3}	3.58×10^{-4}
Uterus	1.86×10^{-4}	2.97×10^{-4}	3.85×10^{-4}
Effective dose	3.34×10^{-3}	1.72×10^{-3}	7.97×10^{-4}

organs are fairly similar between the flow-based and content based models, but the contributions to effective dose due to these differences have a notable effect on the total estimated effective dose.

Due to the short physical half-life of ^{82}Rb, differences are expected between activity distributions in many organs based on either flow or total blood content. Similar issues were encountered and treated for ^{15}O-labeled H_2O by Brihaye et al. (1995). The flow based model of Leggett et al. treats more organs than were evaluated by Ryan et al., but for the organs that were evaluated, agreement with the Leggett et al. model was reasonable, and thus lends credence to the Leggett et al. model. Adoption of the Leggett et al. model is thus proposed, with the modifications noted above regarding dose adjustments for hollow organs. Further minor adjustments to the doses for the hollow organs gallbladder and urinary bladder could be made, but they would be expected to have a small impact on the overall conclusions. The Ryan et al. doses were based on measurements in only two subjects, and the Leggett et al. model is theoretical, thus both have their limitations. However, it is still reasonable to suggest their use in place of the overly conservative ICRP model. Further research and measurements in the future may further improve our understanding of the dosimetry of this agent.

Differences between models of this sort must be made in the context of an understanding of the uncertainty that may exist in these reported values (Stabin 2008a). This was the original impetus for the review article on nuclear cardiology dosimetry; i.e., are the differences between published dose estimates for different nuclear cardiology agents, from different sources truly different, given the uncertainties in standardized dose estimates? In most cases, the differences that are calculated are significant, but when the uncertainty in the values is considered, it is suggested that: “Differences in dose estimates between any two radiopharmaceuticals should be appreciated and considered in the overall planning for the use of various diagnostic techniques, but small differences in dose estimates between radiopharmaceuticals should not be considered decisive in choosing radiopharmaceuticals for broad use in the nuclear medicine population. Considerations such as diagnostic power, ease of use, image quality, patient comfort and other similar factors should generally dictate the choice of a radiopharmaceutical, with radiation dose being only a secondary or tertiary consideration” (Stabin 2008c). Nonetheless, refinement of models to provide the most reasonable reference values is an ongoing process, and in this case did result in a significant change in the recommended effective dose for this agent. Resources such as the ICRP Task Group tables (ICRP 1988) and the RADAR web site (Stabin and Siegel 2003) will change at times as dose models are reviewed and updated, but should be considered reliable sources of standardized dose calculations for routine use.

CONCLUSION

The blood content-based model given in the ICRP report was found to produce dose estimates that were considered to be overly conservative, and the blood flow-based model of Leggett et al. (1996), which showed good agreement with available measured data provided by Ryan et al. (1985), was considered to be more reasonable. The dose estimates given in Table 3 for ^{82}Rb-chloride, based on the Leggett et al. blood flow-based kinetic model, are suggested for general use. The effective dose based on these assumptions is about 1.7×10^{-3} mSv MBq^{-1} administered.

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