A Radionuclide Therapy Treatment Planning and Dose Estimation System

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An object-oriented software system is described for estimating internal emitter absorbed doses using a set of computer modules operating within a personal computer environment. The system is called the Radionuclide Treatment Planning and Absorbed Dose Estimation System (RTDS). It is intended for radioimmunotherapy applications, although other forms of internal emitter therapy may also be considered. **Methods:** Four software modules interact through a database backend. Clinical, demographic and image data are directly entered into the database. Modules include those devoted to clinical imaging (nuclear, CT and MR), activity determination, organ compartmental modeling and absorbed dose estimation. **Results:** Both standard phantom (Medical Internal Radiation Dose [MIRD]) and patient-specific absorbed doses are estimated. All modules interact with the database backend so that changes in one process do not influence other operations. Results of the modular operations are written to the database as computations are completed. Dose-volume histograms are an intrinsic part of the output for patient-specific absorbed dose estimates. A sample dose estimate for a potential ^{90}Y monoclonal antibody is described. **Conclusion:** A four-module software system has been implemented to estimate MIRD phantom and patient-specific absorbed doses. Computations of the doses and their statistical distribution for a pure beta emitter such as ^{90}Y take approximately 1 min on a 300 MHz personal computer.

Key Words: radioimmunotherapy; radionuclide treatment planning; absorbed dose estimation system

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Absorbed dose is usually estimated, because its measurement in vivo is not feasible for routine clinical studies. Recent clinical trends in radionuclide therapy with radiolabeled antibodies have demonstrated the need for more accurate radiation absorbed dose estimates (*1*). For many clinical trials, such estimates are used to decide whether a patient should begin therapy and to prescribe the amount of activity that should be administered. More accurate estimates are also essential for establishing fundamental dose-response relationships for toxicity and efficacy of radioimmunotherapy (RIT). In RIT, absorbed doses are delivered by injecting radiolabeled antibody into the patient. The unique physiological characteristics of each patient limit the possibility of predicting the radioactivity distribution and thus absorbed dose before injection. Rather, a small amount of activity, in a preliminary imaging protocol, is used to estimate biodistribution results.

The process of internal emitter estimation involves three steps: determination of tissue uptake of administered radiopharmaceuticals, modeling to effect temporal integration of the uptake data and simulation of radiation transport in anthropomorphic or patient-specific phantoms. In this article, we discuss an integrated radionuclide treatment planning and absorbed dose estimation system (RTDS) developed at our institute. Although RTDS was designed for RIT, it can be used generally in radionuclide imaging and therapy protocols to provide standard phantom or patient-specific absorbed dose estimates.

MATERIALS AND METHODS

The overall design of RTDS was based on an object-oriented concept. All the components were separated into modules or objects (Fig. 1). RTDS includes two major components: a database subsystem and a calculation subsystem. A relational database was chosen, because it best fit the structure of RIT clinical data. All calculation modules, developed under Microsoft Visual Basic (Microsoft, Redmond, WA) and Microsoft Visual C++, are separated from the database tables. An Intel Pentium II (Intel; Santa Clara, CA) processor (300 MHz) was selected to be the hardware platform because of its low cost. Two 9-GB, duplexed hard drives and 128 MB of central memory were used for this application. Microsoft Windows/NT was chosen as the operating system, because it is a present-day industrial standard.

The database component stores three types of information: demographic/biological data, sample counting results and sequences of images. Demographic/biological data include name, height, weight, date of birth and complete blood chemistry values. Activity levels determined from blood, urine, bone marrow, tumor and tissue biopsies are stored in the patient sample section. Image data include the patient's CT, nuclear medicine (planar and possibly SPECT) and MR images.

Calculation modules were designed to include calculation processes needed to estimate the final absorbed doses from database results. Calculations were separated into individual modules (objects) so that change in one module did not require any

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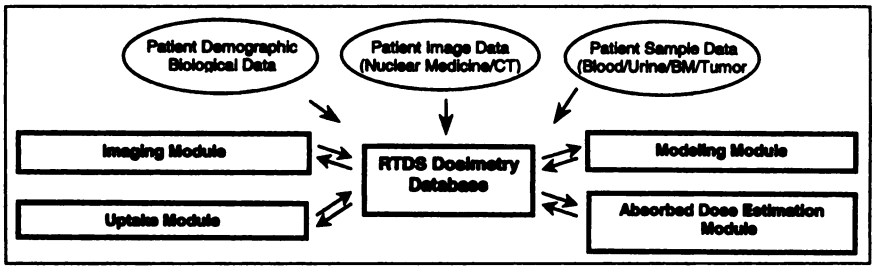

FIGURE 1. RTDS system design for patient receiving monoclonal antibody therapy.

changes in others. Four modules were developed. These include functions for imaging processing, quantitative activity uptake calculations, modeling of activity versus time curves and absorbed dose calculations. With our database backend, transferring information between different parts of the system was transparent to the user. This automated data-handling design allowed minimum user interaction in data entry level and made the final result much less error prone. The only required user inputs are drawing organ regions of interest (ROIs), urine/blood counting with well counters and entering patient demographic data into the database. After that, data processing is integrated entirely to give the final absorbed dose estimates. Another strength of the RTDS is that all raw data, intermediate data during processing and the final results were stored in the system's relational database. Data retrieval, interpatient comparison and cross-protocol comparison are readily accomplished.

Image Module

Nuclear and CT (or MR) images were displayed and processed on the computer using dual 17-in. monitors, which allowed a series of images to be viewed at the same time across the two screens. In RIT image processing, a common task was drawing an ROI around an organ. Thus, our whole-body image processing module in RTDS was tailored for RIT image ROI drawing. Among its features are image tools such as color map manipulation, image zooming and image windowing. It allows the user to draw ROIs with different colors and shapes. These regions can be modified, moved, deleted, archived, retrieved, copied and pasted from one image to another. Processing software constructs and displays count-versus-time curves for each organ ROI. When the user is satisfied, regions and their associated activity values are archived into the database.

Uptake Module

For uptake estimates, the user has three options: the generally accepted geometric mean method (*2*), quantitative SPECT and the newly developed CT-assisted matrix inversion (CAMI) method (*3*). For the CAMI method, CT scans of the patient are processed and organ/tumor ROIs drawn with an auto-edge detection technique. Patient-specific organ and tumor volumes are generated. These three-dimensional volumes are projected onto the coronal plane and fused with nuclear medicine coronal planar images. Given the actual organ volumes and locations, the CAMI calculation of organ and tumor uptake is then performed. The user may use SPECT volumes, if available, as an alternative for organ/tumor mass determinations. All final activity results are saved to the database.

Modeling Module

Three options have been developed for representing and integrating biodistribution data. One may use simple curve fitting with multiple exponential functions (open model). If a closed system is more desirable, the user may opt for a pharmacokinetic model involving cross-coupled organ systems. Finally, if no open or physiological representation is possible, the user may choose to represent time-activity curves via a sequence of trapezoids. Cumulative activities (residence times) for organs are then integrated using one of these three representations. It may be necessary to use more than one technique in a given patient, because all organs may not be included in a given physiological model.

Absorbed Dose Estimation Module

Two methods are available for absorbed dose estimation given the organ residence times. One is based on the standard Medical Internal Radiation Dose (MIRD) phantom set (*4*). With the provision of the relevant S values courtesy of Dr. Michael Stabin (Oak Ridge Associated Universities, Oak Ridge, TN), the MIRDOSE3 algorithm was integrated transparently into RTDS so that dose calculations were streamlined. For example, the user does not need to type the residence times into the MIRDOSE3 program nor need to record final absorbed dose values. All residence times are retrieved from the database, and absorbed doses are archived to the database automatically. This type of standard phantom computation may be appropriate for submission of a human protocol to regulatory agencies such as the Food and Drug Administration.

Our second dose estimation method uses the Monte Carlo-assisted voxel source kernel (MAVSK) algorithm (*5*). With MAVSK, one convolves a Monte Carlo-generated voxel source kernel for the

TABLE 1
Absorbed Dose Estimates (rads/mCi) for ^{90}Y Monoclonal Antibody

	Organ							
	Liver	Spleen	Left kidney	Right kidney	Heart	Left lung	Right lung	Residual body
CAMI and MAVSK	20.81	11.36	5.01	10.93	11.61	2.83	4.47	1.92
GM and MIRDOSE3	18.87	23.01	13.35		12.62	1.09		1.83

CAMI = CT-assisted matrix inversion; MAVSK = Monte Carlo-assisted voxel source kernel; GM = geometric mean.

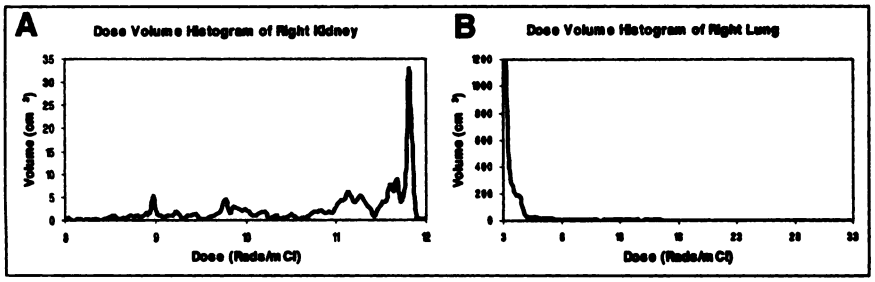

FIGURE 2. Representative dose-volume histograms for the ^{90}Y antibody patient whose mean absorbed doses are given in Table 1. (A) Right kidney. (B) Right lung.

appropriate radionuclide with the patient's activity distribution residence times created by SPECT or CAMI analysis (*3*). Because the convolution is performed over the actual patient geometry, this technique produces a patient-specific organ (or tumor) absorbed dose estimate. Included with the estimate are its SD and dose ranges. Also available are organ dose-volume histograms (*5*). All such patient-specific absorbed dose estimates are saved to the database. Table 1 contains a sample computation comparing MIRDOSE3 and MAVSK results for a potential RIT patient receiving a ^{90}Y monoclonal antibody. Whereas total analysis time was approximately 2 h, almost all computations took place during data acquisition. The majority of time was spent on drawing ROIs and performing the modeling and integrations necessary for residence time determinations. At the end of data taking, absorbed dose estimation took only 1 min on our personal computer (PC) system. Notice that individual (right and left) kidney and lung estimates were determined with the MAVSK method, which included cross-organ dose, e.g., the increased right kidney estimate due to the proximity of the liver. Dose-volume histograms, as shown in Figure 2, were also produced (*5*).

CONCLUSION

RTDS has been designed to be a PC-based treatment planning and absorbed dose estimation system for radionuclide imaging and therapy. It differs from other estimation systems in that it is complete, essentially accomplished during data acquisition and patient-specific. It incorporates every aspect of internal radionuclide therapy treatment planning, including image processing, pharmacokinetic modeling and dose estimation by a database backend. The modular feature with database backend allows minimum human interaction thereby reducing human error. It is designed based on object-oriented concepts, so it can be general and yet flexible. It has built-in standard algorithms, e.g., the geometric mean technique for planar image activity quantitation and MIRDOSE3 for dose estimation. There are also more advanced techniques, e.g., the CAMI strategy for planar image activity quantitation and the MAVSK method for patient-specific absorbed dose estimation.

The fact that RTDS is PC-based allows it to be ported and distributed among different users easily and economically. For RIT, rapid turnaround time and flexibility to do different postcalculation comparisons allow the physicist/physician to perform patient treatment follow-up in terms of assessing the treatment efficacy and normal organ toxicity. Availability of RTDS software could accelerate the dosimetry analysis in clinical trials, reduce potential calculation errors and improve the quality of dosimetry results. Commercial support for the distribution of the RTDS system is being investigated. All of these results imply a possible standard technique for MIRD phantom or patient-specific absorbed dose estimates.

REFERENCES

1. Meredith RF, LoBuglio AF, Spencer EB. Recent progress in radioimmunotherapy for cancer. *Oncology.* 1997;11:979–984.
2. Thomas SR, Maxon HR, Kereiakes JG. In vivo quantitation of lesion radioactivity using external counting methods. *Med Phys.* 1976;3:253–255.
3. Liu A, Williams LE, Raubitschek AA. A CT-assisted method for absolute quantitation of internal radioactivity. *Med Phys.* 1996;23:1919–1928.
4. Stabin MG. MIRDOSE: personal computer software for internal dose assessment in nuclear medicine. *J Nucl Med.* 1996;37:538–546.
5. Liu A, Williams LE, Wong JYC, Raubitschek AA. Monte Carlo assisted voxel source kernel method (MAVSK) for internal dosimetry. *J Nucl Med Biol.* 1998;25:423–433.