In targeted radionuclide therapy, registered SPECT scans are required to obtain the 3D dose distribution following a therapy administration. An iterative, 4D method is presented that allows simultaneous registration of all the acquired scans. The method makes the assumption that the tumour activity-time pattern may be described by two phases, an initial uptake phase and a washout phase. As the first scan is usually acquired on the second or third day following administration, due to radiation protection considerations, the model reduces to a single washout phase described by a single exponential. Each voxel activity-time sequence is fitted to a mono-exponential and the residual error is calculated using the chi-square function. The cost-function is defined as the sum of the chi-square values for all the tumour voxels considered. A simulated 4D set is initially generated based on the reference scan and an estimate of the effective decay (calculated by either the average or the maximum tumour counts of the individual scans). The individual scans are initially aligned exploiting the simulated 4D set information and then the registration is refined using the already transformed scans. A perturbation study was carried out and demonstrated that the 4D method was robust to the choice of the registration starting point. The method was applied to 10 patient therapy studies and resulted in successful registration in all cases. For 5 studies, registration was also carried out using external markers and in 4 of those studies the 4D method resulted in a more accurate registration compared to the marker-based method confirmed by both a smaller chi-square value and visual inspection of the registered sets.

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HIGH DOSE ^{131}I ANTI-CD20 RADIOIMMUNOTHERAPY FOR NON-HODGKIN'S LYMPHOMA: ADJUSTING RADIATION ABSORBED DOSE TO ACTUAL ORGAN VOLUMES.

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High dose radioimmunotherapy (RIT) using ^{131}I labeled anti-CD 20 (B-1) monoclonal antibodies has been used successfully in treating patients with relapsed or refractory non-Hodgkins Lymphoma (NHL). To minimize toxicity to non-marrow organs such as lungs, liver, and kidneys, radiation dose evaluation should be organ specific. Records of all patietns (n=84) who underwent radiation absorbed dose evaluation after a test infusion of ^{131}I-labeled antibodies for RIT between January 1991 and April 2001 were reviewed. Following a trace labeled antibody infusion, serial gamma camera images and whole body NaI probe counting were used within the construct of the MIRD schema to calculate the organ doses and required radioactivity amount for therapy. Escalating dose levels to normal organ receiving the highest radiation absorbed dose were used. Mean residence times in organs were calculated using the time activity curves. We then adjusted the residence time by the ratio of MIRD organ mass to actual patient mass (see table below). The mean radiation absorbed doses cGy/MBq (rad/mCi) were MIRD model – Lungs – 0.16 (5.81); Liver – 0.10 (3.74); Kidneys – 0.10 (3.73); Spleen – 0.26 (9.59); Whole Body – 0.03 (1.05). CT corrected - Lungs – 0.13 (4.77); Liver – 0.11 (3.95); Kidneys – 0.08 (3.06); Spleen – 0.17 (6.24); Whole Body – 0.02 (0.90). This work shows that large variations in patient organ masses can be adjusted using this technique for more accurate dose assessment and better treatment planning.

Organ	Mean Residence Time (Hr) MIRD Model	Mean Residence Time (Hr) CT Adjusted	ρ
Lungs	11.25	9.43	0.39
Liver	11.61	12.4	0.32
Kidneys	2.05	1.76	0.71
Spleen	3.35	2.11	0.12
Whole Body	79.67	69.64	0.82

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THREE-DIMENSIONAL DOSIMETRY FOR REPEATED I-131 mIBG THERAPY OF NEUROBLASTOMA.

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Neuroblastoma patients frequently present with large abdominal masses, and targeted radionuclide therapy (TRT) with I-131 mIBG often results in a heterogeneous distribution of uptake of radionuclide throughout the tissue. Three-dimensional dosimetry is therefore performed using a sequence of SPECT scans. Pre-therapy whole-body dosimetry, incorporating uncertainty analysis, enables administered activities to be optimised on a patient-specific basis. Frequently, repeat treatments are given. However, accurate tumour dosimetry for TRT is difficult to achieve, due mainly to the difficulties of image quantification, although to optimise treatment it is necessary to determine whether successive administrations of activity result in a similar dose being delivered to the target. Image registration of dose distributions resulting from successive therapies has been carried out, using voxel-based methods, to enable direct comparisons to be made on a voxel by voxel basis. The distribution of absorbed dose ratios does not rely on absolute quantification and is therefore independent of these associated errors, which can be significant for I-131. 3 sets of patient data have been studied to date, each of which consist of 2 therapies. In 1 case, a similar activity was administered on both occasions and a similar tumour dose was delivered. In the other two cases a substantially higher activity was given for the second therapy and a correspondingly greater tumour dose was delivered. This demonstrates that within limits defined by whole-body toxicity, higher administered activities can deliver a higher tumour dose. Dose fractionation is therefore a feasible method of treatment that may be planned in advance.

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IMPLEMENTATION OF MCNP-BASED RADIATION TRANSPORT IN RADIOTHERAPY TREATMENT PLANNING WITH PATIENT-SPECIFIC ANATOMIC AND PHYSIOLOGIC DATA.

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We report here preliminary results of extension of our previous work in use of voxel-based anatomic and physiologic data (from MR and SPECT image data) with the MCNP radiation transport software, to use with a clinical system. The GE Millennium "Hawkeye" system permits nearly simultaneous acquisition and automated fusion of patient CT and SPECT images. The Millennium system has been evaluated and calibrated for quantitative planar and SPECT data acquisition for several radionuclides of interest to internal emitter therapy. Import of the image data into the MCNP program was performed using the SCMS interface program, previously demontrated in entry of voxel data from the Yale phantom (J.Nucl. Med. and Health Phys. 2001). For planar studies, we employ an attenuation-corrected geometric mean approach, using multiple symmetric or asymmetric energy windows for scatter correction. For SPECT studies, the GE system uses the Chang method for attenuation correction and the OSEM approach for reconstruction. We also employ an image analysis package developed at Vanderbilt called MIDAS, which provides not only rapid image analysis but semiautomated region

segmentation routines in two and three dimensions. The SAAM II software is routinely used for kinetic analysis of gathered data. The Monte Carlo calculations run in hours to days on a single dedicated workstation; eventually we will exploit distributed computing network capabilities to reduce this time to a few hours. These procedures have been implemented in a limited number of studies to date with patients at our institution. Our intent is to integrate these components into a working system that can provide analysis of patient data in a time frame suitable for evaluation and optimization of patient therapy.

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CELLULAR DOSIMETRY FOR BIOLOGICALLY TARGETED RADIONUCLIDE THERAPY IN VOXEL GEOMETRY.

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For targeted radionuclide therapy, determination of the heterogeneity of dose distribution is important, both at a macroscopic and at a cellular scale. This can have a strong influence on treatment efficacy, to an extent that depends on the radionuclide used. At a multi-cellular scale, heterogeneity will be due to the localisation of the radionuclide within the cell or to complex mechanisms such as the migration of the compound between extra-cellular space and the cell (e.g. mIBG in neuroblastoma treatment). A further aspect to be considered is the amount of 'cold' (i.e. carrier-added) versus 'hot' therapy agent that is administered. A software package has been developed that performs dose calculations from three-dimensional activity distributions by the use of an analytical representation of the point-dose kernel for 131-I. The program has been designed to work within a user-defined voxel geometry, in order to account for non-spherical activity distributions. The size and geometry of the cell and nucleus may be defined, and radionuclide uptake can be considered within the nucleus, the cytoplasm, at the membrane or within the extra-cellular space. Dose distributions calculated using this program varied significantly with activity localisation within the cell, and to a lesser extent, with the cellular geometry. The voxel geometry will be useful to simulate realistic heterogeneous radionuclide distributions at a cellular and/or multi-cellular level and will allow the use of histology data and autoradiography in order to compare the potential benefits of different radioisotopes.

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DEVELOPMENT OF A NEW IN VIVO DOSIMETRY SYSTEM FOR RADIONUCLDE THERAPY.

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A new technique for in vivo dosimetry is under development based on laser induced fluorescence LIF (Optically stimulated luminescence OSL) for radionuclide th Ongoing we are investigating different crystal materials, theoretically calculate dosimetry properties and experimentally verify the dosimetry properties. The techn based on a phenomenon where certain crystals emit fluorescent light when irradiated with laser light. The amount of fluorescence light is proportional to the depos energy / absorbed dose in the crystal. The prompt luminescence is proportional to the dose rate. For in vivo dosimetry small crystals will be optically coupled to th optics. Preliminary experiments have been performed on BaF(Br,I):Eu crystals irradiated with an Ar-laser with excitation wavelength of 457 nm. A linear relations obtained between absorbed dose and dosimeter signal. An electronic device is under development with fibre optical probes coupled to an optical module, laser and computer. To keep the dimension small a dedicated measuring and control computer is developed based on a one-chip computer. Via a serial interface the data are into a PC for further data processing. Different radiation sources have been used for calibration (137Cs, 60Co, low energy X-rays and high energy photons/electro Monte Carlo calculations for different crystals have been performed in a water phantom. As results we have found a good linearity with absorbed dose over five de exponential fading and signal dependence with higher electron/photon energies. In future investigations we will include Al2O3:C as a new crystal material.