Committee Charges for 2011 - 2012:

1. Develop and provide a standardized framework and methodology for calculation of internal dose quantities in nuclear medicine.
2. Compile, evaluate and disseminate data needed to implement standardized internal dosimetry methods including radionuclide decay properties and emissions, energy absorbed fractions and anatomic models.
3. Collect and assess experimental and peer-reviewed data to publish dose estimate reports for selected new radiopharmaceuticals which significantly impact the current practice of nuclear medicine.
4. Provide peer-reviewed evaluations of proposed new dosimetry models and methods including correlating dose with biological response for cellular, animal and clinical trials data.
5. Address other critical and timely dosimetry issues that may impact the current practice of nuclear medicine.
6. Develop, test and publish software and web-based tools that implement MIRD calculation models and techniques including dose-response data and biological effective or equivalent dose quantities.
7. Actively work with other national and international committees through joint meetings and symposia to establish consistency in dosimetry models, techniques, named special quantities and units of dose and biological response.

Current Working Objectives/Goals:

- Continue to develop and publish, for the nuclear medicine community, appropriate scientific methods for calculating internal radiation doses from diagnostic and therapeutic radiopharmaceuticals
- Compile and disseminate supporting data needed to implement such methods, such as radionuclide decay properties and emissions, energy absorbed fractions, and anatomic models
- Develop and publish software tools that implement MIRD calculations and models
- Assess and publish dosimetry for new radiopharmaceuticals
- Develop methods for correlating dose with response in order to evaluate the relevance of factors, in addition to absorbed dose, that influence biological response from internal emitters
- Address other critical and timely dosimetry issues that may impact the practice of nuclear medicine
- Solicit nominations for the annual Society of Nuclear Medicine Loevinger-Berman Award, named in honor of two founding members of the Medical Internal Radiation Dose Committee. Review nominations and elect awardee.
- Further the education of SNM members in dosimetry and related areas by organizing Continuing Education sessions at the annual SNM meetings.

In addition to the overall objectives/goals listed above, a number of task groups have been formed and will be working on projects as summarized in the Appendix.

Progress of Charge/Objectives/Goals to Date (includes items from April 2011 report):

1) Individual MIRD Committee members participate in the following scientific or medical organization activities that relate to the MIRD Committee charges. These activities benefit the Society by directly contributing to and by elevating the profile of SNM and furthering its objectives:
   a) Dr. Zanzonico, a member of the Committee has been tasked by SNM to review the joint ATA, SNM guidelines and patient instructions on radiation safety after radiiodine treatment for thyroid disease.
   b) Dr. Zanzonico recently also co-authored a report on the doses and exposures arising from the Fukushima nuclear reactor incident.
   c) Dr. Fisher participates in the joint ACR/RSNA/SNM Image Wisely campaign.
d) Dr. Zanzonico participates as a member of the U.S. Nuclear Regulatory Commission’s Advisory Committee on the Medical Uses of Isotopes (ACMUI). In response to the continuing efforts by Congressman Edward Markey to roll-back the current regulations on releasability of radionuclide therapy patients to the pre-1997 activity-based criteria (ie the “30-mCi Rule”), Drs. Fisher and Zanzonico were among the principal authors of an ACMUI report to the NRC endorsing the current dose-based release criteria.
e) Dr. Fisher participated on the joint American College of Cardiology/American Heart Association think tank chartered to develop an Action Plan for Radiation Safety in Cardiovascular Medicine.
f) Dr. Howell has been invited by the ICRU to serve on ICRU Report Committee 25, Report Committee on Bioeffects Modeling. This request is a consequence of earlier discussions between MIRD and ICRU.
g) Dr. Sgouros was invited to co-author an application to the European Metrology Research Programme (EMRP) on establishing standards and standard procedures for dosimetry and activity quantification in molecular radiotherapy (MRT). This follows a meeting at the metrology institute in Bern, Switzerland at which Dr. Sgouros was invited to present as a representative of the SNM MIRD Committee. Another application related to discussions with MIRD, “Metrology Support for Biologically Relevant Quantities in Radiotherapy” has also been submitted to EMRP.
h) Dr. Sgouros has been asked to participate in the organization of the radiopharmaceutical dosimetry and therapy meeting to be held in conjunction with EANM in Milan, Italy in autumn of 2012. MIRD Committee membership will participate in the planning of this meeting.
i) Dr. Sgouros delivered the Invited Professor lecture at the FDA in early Dec. 2011 and has been invited to speak at the World Radiopharmaceutical Conjugate Summit in DC in Feb 2012.
j) Drs. Sgouros and Fisher participated in a symposium on alpha-particle emitters in Cancer Therapy held in Berlin, Germany. Dr. Fisher presented work on novel alpha-emitter-retaining constructs and Dr. Sgouros addressed issues related to alpha-particle dosimetry and the need to develop methodologies that provide the dose distribution rather than only the average absorbed dose to a target volume.
k) Dr. Bolch serves as member of Committee 2 of the International Commission on Radiological Protection (ICRP) and serves as Chair of its Task Group on Dose Calculations. Through this appointment, a coordination of dosimetry data, techniques, and dosimetric anatomic models for internal emitters is being coordinated between MIRD and ICRP.
l) Dr. Bolch and Dr. Howell serve as members of the Main Council of the NCRP - National Council on Radiation Protection and Measurements.
m) Dr. Brill serves on the NCRP SC-1-16 Committee finalizing its report on Uncertainty in Radiation Risk Estimates

2) Continue effort to introduce radiobiological modeling in order to relate absorbed dose to biologic effect.

3) MIRD Committee web site now includes latest publications and many of the recent MIRD CME presentations and related JNM publications. Links to SNM revenue-generating monographs produced by the MIRD Committee will also be implemented.

4) The following two MIRD CE sessions were approved for the 2012 annual meeting in Miami, FL; the speakers have been confirmed and all paperwork submitted to SNM:

Sunday, June 10

2:30 PM-4:00 PM A201/202

| Dose Reduction in Pediatric Nuclear Medicine |
| Sponsored by the MIRD |
| CME: 1.5 |
| CPE: 1.5 [210-000-12-135-L04] |
| VOICE A+: 1.5 |
| CAMPEP: 1.5 |

Educational Objectives
Upon completion of this activity, the participant will be able to:
1. Relate nuclear medicine organ dose to nominal values of cancer incidence and mortality.
2. Compare methods of standardized nuclear medicine dosing in pediatric imaging from both Europe and North America.
3. Recognize potential role of body morphometry in determining image quality/risk optimized pediatric dosing.

Organizer: Wesley E. Bolch, PhD
Moderator: S. Ted Treves, MD
Co-Moderator: Frederic H. Fahey, DSc

2:30 PM - 2:55 PM BEIR VII Cancer Risk Models and Their Revisions for Patient Medical Dosimetry Wesley E. Bolch, PhD
Pediatric Dosing Guidance - Europe and North America
Michael Lassmann, PhD; S. Ted Treves, MD

Future Directions for Individualized Pediatric Dosing Guidance - MIRD Committee
George Sgouros, PhD

Review of Session and Self-Assessment
Wesley E. Bolch, PhD

4:15 PM-5:45 PM
Radiation Protection in Nuclear Medicine

Sponsored by the MIRD

CME: 1.5  VOICE: 1.5
CPE: 1.5 [210-000-12-140-L04]  CAMPEP: 1.5

Educational Objectives
Upon completion of this activity, the participant will be able to:
1. Quantify the stochastic risk and effective dose to patients undergoing either diagnostic imaging or therapy.
2. Understand current NRC regulations and their potential changes regarding dose limits to nuclear medicine staff.
3. Develop rigorous methods of reporting patient risk in IRB protocols and in clinical trial design.

Organizer: Wesley E. Bolch, PhD

Moderator: Wesley E. Bolch, PhD

Co-Moderator: Roger W. Howell, PhD

4:15 PM - 4:20 PM
2012 MIRD Loevinger-Berman Award
Pat B. Zanzonico, PhD

4:20 PM - 4:45 PM
Evolution and Use of Effective Dose - Review of ICRP Publications 26, 60, and 107
Wesley E. Bolch, PhD

4:45 PM - 5:10 PM
Proposed Changes in NRC Dose Limits - Annual Effective Dose and Equivalent Dose to Eye Lens
Pat B. Zanzonico, PhD

5:10 PM - 5:35 PM
Quantifying Patient Risk in IRB Protocols and Clinical Trial Design
George Sgouros, PhD; Ruby F. Meredith, MD, PhD

5:35 PM - 5:45 PM
Discussion/SAM
Wesley E. Bolch, PhD

5) On the recommendation of the MIRD Committee and pending approval of the SNM Awards Committee, Dr. John Humm of Memorial Sloan-Kettering Cancer Center will receive the 2012 Loevinger-Berman Award.

6) On September 1, 2011 we welcomed Mark Dunphy, DO, from Sloan-Kettering Cancer Center, and also a member of the SNM YPC to the MIRD Committee. We personally welcomed our newest Committee member at our March meeting in Nashville.

7) The MIRD Committee continues to generate new S values for radionuclide dosimetry through a joint effort with IAEA and the University of Florida.

8) The IAEA funded Ande Bao’s internship project on bone marrow dosimetry for Lu-177 phosphate as a bone pain agent. Dr. Bao will work with Dr. Zanzonico on the dosimetry of bone lesion palliation therapy with 177Lu-EDTMP.
This is an effort that is of interest to the IAEA, since 177Lu is a therapeutic radionuclide which is relatively inexpensive and widely available internationally. The project involves experimental (animal) work that Dr. Zanzonico has agreed to host at Memorial Sloan-Kettering Cancer Center (MSKCC) and also partially subsidize in terms of animal animals and instrumentation. In light of SNM’s current budgetary constraints, funding from the IAEA has been secured from the IAEA (in the form of Research Contract) to support Dr. Bao’s travel to and room and board in New York City. This project is on hold, however, until certain administrative issues are resolved and the funds are actually transferred from the IAEA to Dr. Bao’s institution, University of Texas Health Science Center at San Antonio. At the same time, Dr. Zanzonico’s Small-Animal Imaging Core Facility at MSKCC will be replacing shortly its existing XSPECT rodent microSPECT/microCT with an NIH (S10 grant)-supported higher-sensitivity, higher-resolution nanoSPECT microSPECT/MicroCT, enhancing the technical capabilities that will be used for Dr. Bao’s project.

9) The MIRD Committee continues to prepare various pamphlets on medical internal radiation dose as needs arise in the community:
   a) The committee is currently revising a follow-up report to Pamphlet 21 that described a dosimetry formalism adopted by the ICRP. The follow-up will address questions related to the effective dose and discuss a formulation that is clearer and more relevant to nuclear medicine dosimetry.
   b) A pamphlet on 3-D dosimetry/image quantification (Pamphlet 23) is in press, JNM.
   c) Other Pamphlets (still at very early stage), include: Hybrid phantoms and skeletal models, Therapeutic Radiopharmaceutical Activity Administrations and BED Modeling, Regional and Interstitial Therapies, and Patient-to-Family Member Doses. A task group to generate a radiobiological reference human that will compile radiobiological data for use in radiobiological modeling of radionuclide doses is being formed. (See Task group summary in Appendix).
   d) We are preparing a new dose estimate report for iodine-131 tositumomab (Bexxar).

10) The MIRD Committee continued to develop an online dose-response tool for determining potential toxicity to kidney from radionuclide therapy. During this evaluation period, the program is running on a web server at Case Western Reserve University. This new dosimetry tool is an interactive version of MIRD Pamphlet No. 20: The Effect of Model Assumptions on Kidney Dosimetry and Response—Implications for Radionuclide Therapy. J Nucl Med 2008; 49:1884-1899. This tool was developed by MIRD Committee Intern Ann Larkin working under the mentorship of Dr. Barry Wessels.
   a) We recently added a feature to investigate fractionation.
   b) Beta-testing of locked down version of the dose-response tool through the Case server is ongoing and input from three non-committee investigators has been obtained.
   c) SNM website testing of the on-line tool is planned for June 2012.

11) We developed a new web-based tool for cellular and multicellular dosimetry. We are testing the dosimetry tool at the New Jersey Medical School, University of Medicine and Dentistry (http://njmsweb04.umdnj.edu/). We anticipate readiness of the dosimetry tool for on-line launch on the SNM website by the fall of 2012 in tandem with a short communication in the Journal of Nuclear Medicine.

12) The IHE (Integrating the Healthcare Enterprise) is defining how radiology equipment vendors should include an automatic radiation dose report along with the images when acquiring patient studies. The goal of this is to be able to easily report radiation dose, both for individual patients, and for site-to-site comparisons. This will soon include nuclear medicine and PET. The procedure for reporting and gathering this information is defined in an IHE Profile, call the Radiation Exposure Monitoring (REM) profile. This profile is already written for CT and plain radiography. Per a request of Dr. Jerry Wallis, the SNM representative to the IHE, to Dr. Sgouros, Pat Zanzonico has volunteered to serve as the SNM/MIRD representative to the IHE to help draft and review the forthcoming profile.

13) Because of the rising importance of SNM initiatives with the government, a new Commission on Government Affairs has been created and the Commission has two committees:

   1. **Committee on SNM/ACNM Joint Government Relations**: Chair Bob Atcher
   2. **Committee on Coding and Reimbursement**: Chair Gary Dillehay

   ii) Pat Zanzonico was been asked by immediate past SNM President Dominique Delbeke to serve on the Committee of SNM/ACNM Joint Government Relations and has agreed to do so.

The IHE (Integrating the Healthcare Enterprise) is defining how radiology equipment vendors should include an automatic radiation dose report along with the images when acquiring patient studies. The goal of this is to be able to easily report radiation dose, both for individual patients, and for site-to-site comparisons. This will soon include
nuclear medicine and PET. The procedure for reporting and gathering this information is defined in an IHE Profile, call the Radiation Exposure Monitoring (REM) profile. This profile is already written for CT and plain radiography. Per a request of Dr. Jerry Wallis, the SNM representative to the IHE, to Dr. Sgouros, Pat Zanzonico has volunteered to serve as the SNM/MIRD representative to the IHE to help draft and review the forthcoming profile.
APPENDIX – CURRENT MIRD TASK GROUPS

Bolch

Task Group 1 (TG1) Title
MIRD Task Group on Alternatives to the Effective Dose for Quantifying Stochastic Risk from Low-Dose Medical Imaging

Suggested Membership
Bolch (Chair), Brill, Howell, Sgouros, Wessels, Zanzonico
David Pawel (Radiation Protection Division, EPA), Andres Abadia (UF medical physics)

Goals and Objectives
To develop alternative dose quantities for concisely expressing the stochastic risks, as well as the clinical benefits, from medical imaging using ionizing radiation. The task group will work with David Pawel of the US EPA who is implementing updated risk models from the NAS BEIR VII report to give age and gender dependent values of lifetime attributable risk (LAR) for both cancer incidence and cancer mortality for low-dose radiation of individual tissues and organs. Age dependence will be given at yearly increments in contrast to the 5-year increments of BEIR VII. The task group will also address inherent uncertainties with these models as guided by ongoing work of the NCRP. Examples of stochastic risk will be given for both nuclear medicine and CT imaging of patients of varying age and both genders.

Targeted Deliverables
- MIRD Pamphlet as a follow-on to MIRD Pamphlet No. 21
- Possible implementation in MIRD website software

Timeline for Completion
Review of LAR tables – June 2012
Draft pamphlet – July 2012
Submission to JNM – September/October 2012
Task Group 2 (TG2) Title
MIRD Task Group on Hybrid Phantoms and Skeletal Models

Suggested Membership
Bolch (Chair), Brill, ...
Choonsik Lee (NCI), Deanna Pafundi (Mayo Clinic), Mike Wayson (UF)

Goals and Objectives
To develop a series of hybrid (NURBS/PM based) phantoms representing the ICRP series of reference phantoms – newborn, 1-year, 5-year, 10-year, 15-year, and adult. Additional phantoms will be developed covering a broad series of height and weight percentiles (10th to 90th). The phantoms will include a complementary skeletal tissue and dosimetry model giving (1) absorbed fractions for internal electron sources, (2) absorbed fractions for internal alpha particle sources, and (3) dose-response functions for both internal and external photon sources. Voxelized versions of these phantoms will be used to establish a comprehensive database of SAF values for internal photon and electron sources. This database will be used as the basis for a future MIRD web-based software tool.

Targeted Deliverables
• MIRD Pamphlet on Age-Dependent Skeletal Dose Models
• MIRD Monograph on Radionuclide S values
• MIRD website software

Timeline for Completion
• Summer 2012 – completion of pediatric skeletal models
• Fall 2012 – MIRD Pamphlet for age-dependent skeletal dose models
• Summer 2013 – MIRD Monograph on radionuclide S values
Task Group 3 (TG3) Title: MIRD Pamphlet No. 23
Quantitative methods for 3D patient specific dosimetry in internal emitter therapy
Yuni Dewaraja (University of Michigan), Michael Ljungberg (Lund), Eric Frey (John Hopkin's), George Sgouros, Randy Brill (Vanderbilt)

The report will describe methods for quantification of activity and activity distribution in targets for accurate estimation of 3-D absorbed dose from internal emitters. The desired endpoint could be dosimetry for targeted therapy treatment planning, dosimetry for correlation with biological response or dosimetry for approval of new imaging agents. The report will focus on quantitative imaging methods that provide accurate non-uniform radioactivity distributions at the voxel-level for 3D dosimetry. Hence, SPECT, PET and hybrid methods combining 3-D imaging with planar imaging will be discussed.

In Press, JNM
**Task Group 4 (TG4) Title**
MIRD Task Group on Dose Estimate Report for Iodine-131-Tositumomab (Bexxar ®)

**Suggested Membership**
Darrell Fisher (Chair), Ruby Meredith, Yuni Dewaraja, Ajay Gopal
Affiliate Members: Richard Wahl

**Goals and Objectives**
- To develop a dose estimate report for iodine-131-Tositumomab (Bexxar ®) for publication as a MIRD Dose Estimate Report for *JNM*
- To update the dose estimates using current FDA-approved software
- To describe the biological uptake, retention, and clearance of the antibody carrier Tositumomab
- To confirm the product package insert dosimetry or to provide new dose estimates based on multi-institution data

Bexxar, approved by the US Food and Drug Administration in 2003, is a radiopharmaceutical for treating B-cell follicular lymphoma. Bexxar employs an IgG2a anti-CD20 murine monoclonal antibody directly labeled with iodine-131. The antibody Tositumomab binds specifically to the CD20 (human B-lymphocyte-restricted differentiation antigen, Bp 35 or B1). This antigen is a transmembrane phosphoprotein expressed on pre-B-lymphocytes and at higher density on mature B-lymphocytes. The antigen is also expressed on more than 90% of B-cell non-Hodgkin's lymphomas. The recognition epitope for Tositumomab is found within the extracellular domain of the CD20 antigen. CD20 does not shed from the cell surface and does not internalize following antibody binding. Tositumomab is administered sequentially, first as Tositumomab, and then by the radiolabeled iodine-131-Tositumomab. Clinical experience has established the efficacy of the Tositumomab/iodine-131-Tositumomab regimen in patients with relapsed or chemotherapy / retuxan-refractory disease. This drug combination is manufactured by GlaxoSmithKline.

**Patient Data**
We propose three participating institutions: University of Washington-Seattle, University of Michigan-Ann Arbor, and University of Alabama-Birmingham. All patient data will be obtained only from diagnostic infusion, pre-therapy imaging studies. The University of Washington data comprise organ uptake fractions at four time points for the lungs, liver, spleen, kidneys, heart content, and thyroid (blocked), as well as whole-body retained fractions at these same time points, together with organ and patient weights. The patient database includes those that received the centrally-labeled (commercial) Bexxar and is complete for four groups: males (ages 18 – 59 years, n=27), males (ages over 59 years, n=14), females (ages 18 – 59 years, n=27), and females (ages over 59 years, n=4). All trace-labeled (5 to 10 mCi I-131) antibody biodistribution data were obtained by gamma camera imaging before therapeutic infusion. Sponsor approval is not necessary to use these patient data for follow-up dosimetry studies. Ruby Meredith will report on the status and availability of the University of Alabama patient data, and Yuni Dewaraja will report on the status and availability of the University of Michigan patient data.

**Targeted Deliverables**
- MIRD Dose Estimate Report

**Timeline for Completion**
- December 2010 – collection of patient data
- April 2011 – analysis of patient data
- September 2012 – first draft of dose estimate report
- April 2013 – submission to *JNM*
Task Group (TG5) Title
MIRD Task Group on Cellular and Multicellular Radiobiology and Dose Modeling

Current Membership
Howell (Chair), Bolch, Fisher, Sgouros, Wessels.

Goals and Objectives
The aim of this Task Group is to develop an interactive, web-based application which implements cellular and multicellular dosimetry models described in the MIRD Cellular S Values monograph and in Goddu et al. (J Nucl Med, 35, 521-30, 1994). This application will build in radioactivity distribution models and radiobiological response models to provide the user dose-response information for various multicellular geometries.

Deliverables
1) Educational web-based modeling tool for estimating dose-response for cellular and multicellular tissues that contain radioactivity.

Timeline for Completion

- 2007-2011 – Version 1.0 – limited scope tool that calculates S values for cellular self- and cross-dose. This Java applet runs openly for beta testing on a UMDNJ web site (http://njmsweb04.umdnj.edu/) – completed by Han Wu. Functionality includes:
  o Selectable source radioactivity
    ▪ Monoenergetic electrons
    ▪ Monoenergetic alpha particles
    ▪ Full radiation spectra for the radionuclides in the 1989 MIRD Radionuclide Data and Decay Schemes.
    ▪ Selectable average radiation spectra for the radionuclides in the 2007 MIRD Radionuclide Data and Decay Schemes.
    ▪ Creation of custom radionuclide that can be saved on user's computer.
  o Selectable radii for cell and cell nucleus.
  o Selectable distance between source and target cell.
  o Selectable source location (cell, nucleus, cytoplasm, cell surface)
  o Selectable target volume (cell, nucleus, cytoplasm)
  o Graphic user interface that displays geometry, selectable options, input and output data
  o Improve computational speed by reducing output to only that specified by user
  o Revise graphic user interface to me more intuitive
  o Permit radii with real numbers (Version 1.0 only allows integer values)
  o Add graphic progress meter to inform user about status of calculation
  o Operational testing by MIRD Committee
  o Implementation on SNM web site or add SNM link to UMDNJ web site
  o Add multicellular capability for planar and geometries
  o Add radioactivity distribution models (uniform, lognormal, etc.)
- 2014 – Version 3.0
  o Add dose response models
**Task Group 5 (TG6) Title**
MIRD Task Group on the influences of thyroid blocking and other factors on thyroid dosimetry of I-131-radiouclide conjugates

**Suggested Membership**
Meredith (Chair), MIRD members, John Pagel (UWash), Sui Shen (UAB)

**Goals and Objectives**
A wide variation of thyroid mGy/MBq even among patients with similar disease, and the same blocking regimen (Bexxar, CC49) has been observed and despite various measures to block I-131 uptake in the normal thyroid from I-131-radiouclide conjugates, concentration and absorbed dose often exceeds that of target(tumor) and all other organs. This can result in thyroid dysfunction, and increase the risk of thyroid cancer.

Objective: To determine the efficacy and influences of various thyroid blocking regimens and other factors on uptake of radioactive iodine (I-131) from I-131-conjugates used in non-thyroid cancer therapy studies.

Methods: Quantitative dosimetry will be calculated using serial planar gamma camera images for patients with one or more exposures to I-131 conjugates. The ratio of each patient’s thyroid dose to whole body and other organ dosimetry will be assessed. Comparison will be made of cGy/MBq to thyroid versus other organs of the same patient and between patients. Factors considered include: iodine thyroid blocking regimens, time from initiation of blocking to I-131-conjugate, total days blocked, 1st, 2nd, 3rd, etc treatment, medicines that may influence thyroid function (eg synthroid), any indication of non-compliance with blocking agents, history of thyroid disease or abnormal laboratory values pre-treatment, effective whole body and plasma half-times of I-131-conjugates, prior radiation to thyroid, amount of I-131 (myeloablative vs lower dose), and renal function.

**Targeted Deliverables**
- MIRD Pamphlet
- Related on-line material

**Timeline for Completion**
- 9/11 obtain IRB approval **DONE**
- 10/11 finalize data collection requests **DONE**
- Completion dates pending
Task Group (TG7) Title
MIRD Task Group on The Radiobiological Reference Human (RHH).

Proposed Membership (italic = Confirmed)
George Sgouros (Chair, RRH TG),
Barry Wessels (Co-Chair, RRH TG),
Sebastien Baechler (CHUV, Lausanne, Switzerland),
Wesley Bolch (MIRD, liaison to ICRP),
Marta Cremonesi (European Institute of Oncology, Milan, Italy),
Roger Dale (Imperial College, London, UK),
Marion DeJong (Erasmus University Medical Center Rotterdam, The Netherlands),
Alla Guseynova (Hopkins, Research Information Technology Systems, RITS),
Robert Hobbs (JHU, Baltimore MD),
Roger Howell (MIRD, liaison to ICRU),
Joe O'Donoghue (MSKCC, NY),
Senthamil, Srinivasan (JHU, Baltimore MD),
Lidia Strigari (Regina Elena National Cancer Institute, Rome, Italy),
Ellen Yorke (MSKCC, NY).

Goals and Objectives
In analogy to the ICRP reference man compilation of organ masses, compositions, and dimensions we propose a Reference Radiobiological Human (RRH) database. A credentialed database of radiobiological parameters to standardize radiobiological model parameter values for different normal organs and tumor types. Table 1 summarizes the values that we envision capturing for use in RPT and possibly XRT dosimetry/radiobiology. Until radiobiological parameters can be measured in individual patients, standardization will be important to enable cross-comparison of dose calculations and radiobiological results.

Table 1 – Parameters for the RRH database (for each organ)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\alpha$ Gy$^{-1}$</td>
<td>the radiosensitivity per unit dose</td>
</tr>
<tr>
<td>$\beta$ Gy$^{-2}$</td>
<td>the radiosensitivity per unit dose squared</td>
</tr>
<tr>
<td>$\mu$ s$^{-1}$</td>
<td>the repair rate constant assuming exponential repair of DNA lesions</td>
</tr>
<tr>
<td>$D_{50}$ Gy</td>
<td>the absorbed dose which if delivered uniformly, leads to a 50% organ complication rate in 5 years</td>
</tr>
<tr>
<td>$k$ Gy$^{-1}$</td>
<td>the slope parameter of the dose vs complication curve as fit by the logistic model</td>
</tr>
<tr>
<td>$W$</td>
<td>Wiki field for on-line, editable commentary</td>
</tr>
</tbody>
</table>

Each parameter will be stored within a multi-row, matrix so that each parameter value is accompanied by a date stamp, commentary, reference to the literature values, etc. The data stamp will preserve previous parameters for back reference when necessary. Parameters will be compiled for normal organs and also for different tumor types.

In support of macro to micro (M2M) modeling:

2. The M2M database: Either within RRH or as a separate database, M2M will hold equations describing an idealized model of the relevant micro-level structure of the organ for different normal organ/radiopharmaceutical combinations. The parameters, $\alpha$, $\beta$, and $\mu$ of the target cell population and fraction of the decays in the macro ROI that should be assigned to the micro source volume will be included (table 2)

Table 2 – Parameters for the M2M database (for selected organ/radiopharmaceutical combinations)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$F(x,y,z,p_i)$</td>
<td>Equation describing micro model, characterized by parameters, $p_i$</td>
</tr>
<tr>
<td>$f(s,t_i)$</td>
<td>Fraction of decays in source, $s$ that are assigned to micro target volume, $i$.</td>
</tr>
<tr>
<td>$\alpha$ Gy$^{-1}$</td>
<td>the radiosensitivity per unit dose for micro region or cell population</td>
</tr>
<tr>
<td>$\beta$ Gy$^{-2}$</td>
<td>the radiosensitivity per unit dose squared for micro region or cell population</td>
</tr>
<tr>
<td>$\mu$ s$^{-1}$</td>
<td>the repair rate constant assuming exponential repair of DNA lesions for micro region or cell population</td>
</tr>
</tbody>
</table>
Each tissue entry in the RRH or M2M databases will include a narrative similar to that found in ICRP 23 Task Group on Reference Man.

**Targeted Deliverables**
- MIRD Pamphlet
- Radiobiological Reference Human (RHH) database
- Relevant micro-scale geometry of selected organs (M2M database)
- On-line access with wiki commentary functionality

**Timeline for Completion**
- 6/2012 – define: scope of work, membership, organ list, radiopharmaceutical list, on-line platform
- 9/2012 – database structures, data entry web site established, organ/M2M sub-committees identified, web site beta testing begins
- 6/2013 – RHH and M2M databases completed
- 12/2013 – Databases with wiki functionality go live.

**UPDATES**
- Initial scope confined to RRH: M2M will be implemented after RRH
- Majority of invited participants have confirmed; awaiting confirmation on 6.
- First on-line meeting planned for late Feb or early March 2012 (before March Committee meeting)
Wessels

Task Group (TG8) Title
MIRD Task Group on Kidney Radiobiology and Dose Modeling

Current Membership
Wessels (Chair), Larkin, Bolch, Cremonesi, Hamilton, Zheng, Bodei, Dale, Meredith, Sgouros, and Howell.

Goals and Objectives

The aim of this Task Group is to develop an educational, interactive, web-based application which implements the kidney dose-response model described in MIRD Pamphlet No. 20: The Effect of Model Assumptions on Kidney Dosimetry and Response - Implications for Radionuclide Therapy (Wessels et al. 2009). This application models the multiregional internal dosimetry of the kidneys combined with the biologic response parameters to predict radiation toxicity to the kidneys. Regionally based surviving fractions for the kidney cortex and medulla are calculated in terms of their concentration ratios for various radiopharmaceutical uptake and clearance. The interactive web application calculates the surviving fractions based on the following definable parameters: volume of the cortex and medulla, radiopharmaceutical, irradiation time, repair half-time, absorbed dose and tissue alpha/beta values of the medulla and cortex. The user may use the default values provided or enter patient specific values to evaluate different theoretical scenarios of radionuclide therapy delivery effect on kidney function modeled in humans.

Deliverables

1) Educational web-based modeling tool for estimating dose-response for kidney toxicity associated with radionuclide therapy.
2) Revaluation of current clinical toxicity data in comparison to modeling results from user group
3) Evaluation of the impact of fractionation (multiple administrations) on the reduction of kidney toxicity in terms of radiobiologic equivalent doses.

Timeline for Completion

2) Development and functional specs – Review interaction and plan (Larkin) with SNM web master and staff liaison (Jermy Ong/Janette Merrill) – by March 2011
3) Testing – Parameter scale, single and multiple point failure and redundancy evaluation - Internal and external to committee, 3 beta test sites – (2 sites completed testing – June 2011) – Wessels et al.
4) Implementation – on to SNM site – restricted password – Sept 2011
5) Roll-out to SNM membership - disclaimer and consult with SNM legal – Sept 2012
Task Group on Bone Pain Palliation Agents

Task Group (TG9) Title: In conjunction with Dr. Bao’s project described above
Clinical Dosimetry for Maximum Tolerated Activity-Based Palliation of Painful Skeletal Metastases Using Bone-Seeking Radiopharmaceuticals

Suggested Membership List
Ande Bao, Wes Bolch, Ruby Meredith, Pat Zanzonico

Goals and Objectives
To develop a widely applicable (eg gamma camera imaging-based) dosimetry algorithm to derive patient-specific maximum tolerated activities (MTAs) for radiopharmaceutical palliation of painful bone metastases, taking into account the actual partitioning of such agents between cortical and trabecular bone in deriving the red marrow dose (generally the therapy-limiting normal tissue).

Targeted Deliverables
1) Peer-review publication on IAEA-supported animal study by Ande Bao (MIRD Intern) to determine the partitioning of Lu177-EDTMP (+ other bone agents?) between cortical and trabecular bone
2) A MIRD Report (peer-reviewed publication)
3) On-line dosimetry tool for calculation of patient-specific MTAs based on foregoing partitioning data and serial whole-body activity measurements

Current Status
The project is on hold, however, until certain administrative issues are resolved and the funds are actually transferred from the IAEA to Dr. Bao’s institution, University of Texas Health Science Center at San Antonio. This should be resolved shortly and experimental work begun before the end of the year.
Note: In part, in response to Congressman's Markey's ongoing efforts to roll back release criteria for radionuclide therapy patients to the previous activity-based criteria)

**Task Group Title**
Estimation of Radiation Doses to Family Members, the General Public, and Other Potentially Exposed Cohorts from Radionuclide Therapy Patients

**Suggested Membership List**
Wes Bolch, Randy Brill, Darrel Fisher, Ruby Meredith, Pat Zanzonico

**Goals and Objectives**
To develop reference data - patient-to-family member, -co-worker, -co-traveler, -hotel and other service worker “S factors” as functions of isotope, body size, posture, distance, and “shielding” - and a general calculation algorithm for estimation of the radiation doses to family members and other potentially exposed cohorts from radionuclide therapy patients post-release from the hospital

**Targeted Deliverable**
1) “Preliminary” peer-review publication(s) on cohorts of greatest concern, co-worker, -co-traveler, -hotel and other service worker
2) A MIRD Report (peer-reviewed publication)
3) On-line dosimetry tool for calculation of dose-based releasability and duration of precautions (prohibition on certain activities) for radionuclide therapy patients

**Current Status**
Still on the “drawing board”
TG11: Task Group on Regional and Interstitial Therapies

Task Group Title
Estimation of Radiation Doses to Targeted and At-Risk Normal Tissues for Regional Radionuclide Therapies

Suggested Membership List
Yuni Dewaraja, Roger Howell, Ruby Meredith, Barry Wessels, Pat Zanzonico

Goals and Objectives
To develop reference data - source volume-to-target and-at-risk normal organ “S factors” as functions of isotope, volume size, volume shape, target depth, and normal organ (including size (age)-dependence) - and a general calculation algorithm for estimation of the radiation doses to targeted surfaces and/or volumes and at-risk normal organs from interstitial, intra-cavitary, and other regional radionuclide therapies.

Targeted Deliverables
1) A MIRD Report (peer-reviewed publication)

Current Status
Still on the “drawing board”