

This report was written in October, 2000 an ad hoc working group and is an initial report on Biological and Functional Imaging to the AAPM's Radiation Therapy Committee. The Ad Hoc Working Group is now the Molecular Imaging in Clinical Radiation Oncology Sub-Committee of the RTC. The membership is now:

Dan Bourland, Chair, Wake Forest University, Winston-Salem, NC
Isaac Rosen, Univ. of Texas M.D. Anderson Cancer Center, Houston, TX
Zuofeng Li, University of Florida, Gainesville, FL
Christopher Scarfone, Vanderbilt University, Nashville, TN

Additions and revisions to the membership are being considered by the RTC at the July, 2002 AAPM meeting in Montreal.

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Radiation Therapy Committee of the AAPM
Ad Hoc Working Group on Biological and Functional Imaging in Radiotherapy

Report to the Radiation Therapy Committee
ASTRO, Boston, MA
October 22, 2000

Membership

The members of the Ad Hoc Working Group on biological and functional imaging in radiation therapy treatment planning are:

Isaac Rosen, Chair, University of Texas M.D. Anderson Cancer Center, Houston, TX
Dan Bourland, Wake Forest University, Winston-Salem, NC
Zuofeng Li, University of Florida, Gainesville, FL
Christopher Scarfone, Vanderbilt University, Nashville, TN

The first meeting of the working group was held at the 2000 annual meeting of the AAPM in Chicago. Subsequently, the working group communicated via e-mail and telephone.

Charge of the Ad Hoc Working Group

The working group was charged with developing a proposal for creating a permanent vehicle within the RTC to direct AAPM's efforts in promoting and influencing new developments in these areas of image-guided therapy. The proposal should include a detailed charge for the vehicle and recommendations for appropriate representation from other Science Council committees.

Molecular Imaging for Clinical Radiation Oncology

Biology and medicine are converging into what is being called "molecular medicine". This is loosely defined as medicine that utilizes molecular information to design treatment strategies. As pointed out recently by Dr. Klausner at the National Cancer Institute, the link between biology and physics in the 21st century will be cancer[1]. With new hybrid x-ray CT/molecular imaging scanners capable of providing fusion data (e.g., CT + PET) becoming commercially available, it is clear that the role of molecular imaging in cancer therapy will continue to increase. It has been projected that 60% - 70% of all imaging studies performed 5 to 10 years from now will be fusion studies.

The term "molecular" is used to refer to images that visualize molecular processes as opposed to structural and anatomic images of tissues and organs. Molecular images include nuclear medicine (planar imaging, SPECT, PET) and MR (fMRI, MR spectroscopy). These images contain information about metabolic and biochemical processes, about tumor physiology, and about normal and abnormal organ and tissue function. Because they describe biological functions, the use of these images in radiation oncology is sometimes termed "functional treatment planning". Molecular images have been used or proposed for the following applications in therapy (e.g.,[2,3]):

- functional MRI to define eloquent regions of the brain or to detect tumor vascularity[4],
- gamma camera images to measure lung perfusion[5],
- MR spectroscopy with contrast enhancement to detect tumor and surrounding tissue characteristics,
- diffusion-weighted MR to image normal and abnormal physiological states,
- nuclear magnetic resonance (NMR) to image elevated choline levels in the prostate,
- NMR spectroscopy of ^{31}P to measure tumor “energy” status to correlate with tumor hypoxia,
- FDG-PET for target volume definition to assess outcome and recurrence[4],
- ^{11}C or ^{124}I PET and ^{131}I SPECT to identify areas of cell proliferation,
- ^{11}C -labeled choline or methionine to identify protein synthesis,
- Annexin V SPECT and PET to image programmed cell death (apoptosis),
- fluorinated misonidazole (PET) or ^{131}I -labeled azomycin arabinocide (SPECT) to examine hypoxia in lung[6], head and neck, and brain[7],
- SPECT to identify regions of good blood flow in patients with COPD, and
- SPECT/PET imaging to study the efficacy of radiation-targeted drug delivery systems in animal models.

For radiation oncology purposes, molecular imaging that improves identification of tumor cells will be used to more accurately define target volumes for individual patients. Molecular imaging to assess the response to therapy may improve the prediction of tumor and normal tissue responses – initially for populations of patients and later for individual patients. Together these data will help in the formulation of biological response models and may assist in the development of computer-optimized treatment plans that maximize the therapeutic ratio for patients. Treatment planning with molecular images will require image transmission, processing, fusion and display[8,9]. Therefore, issues of patient immobilization and motion, image file formats, registration algorithms, and software tools for processing and display will have to be addressed.

A fundamental understanding of the physical and technical factors that affect the qualitative appearance and numerical accuracy and precision of molecular images is needed to safely and meaningfully apply these images to therapy applications. In other words, what is the biological significance of the intensity level of a particular voxel and how is that intensity level affected by the imaging technique? Molecular imaging will certainly be used to assist in identifying cancerous tissues in the body. The “biological attributes” of tumor and normal tissues cannot be assessed accurately if the information in the molecular images is biased. For typical diagnostic applications molecular images do not need to be quantitatively accurate. Common image artifacts affecting the accuracy of diagnostic SPECT and PET images are routinely “read through” by the attending radiologist. However, if image artifacts were mistaken for areas of active tumor, they would be erroneously targeted for increased radiation dose, with potentially serious negative consequences. The accuracy and precision with which molecular imaging techniques permit localization of regions for increased dose targeting and response assessment depend heavily on the acquisition technique, the image processing, and the display method.

Another role of molecular imaging in therapy will be for dose-response analysis of both normal and tumor tissues (i.e., therapy assessment). If molecular imaging data is not quantitatively precise and accurate, then dose-response estimates will be biased which will, in turn, lead to biased assessments of therapeutic response. Furthermore, if molecular images are processed differently from one clinic to another, dose-response data based will be very difficult to interpret or possibly meaningless. Recommendations for processing techniques and parameter values would help standardize the use of molecular images.

Each molecular imaging modality is unique and will probably require specialized quality assurance and quality control. Some imaging studies may even require individual calibration or quality assurance testing for each patient. This situation is similar to other aspects of radiation oncology in which QA is tailored to the treatment technique and dose and/or beam geometry verification is done for each patient (e.g. stereotactic radiosurgery, IMRT). Standardized phantoms and QA tests and benchmark data for each imaging modality for a variety of lesion locations would be extremely valuable in helping users detect and/or avoid errors in image acquisition, image processing, and image application to therapy.

Another area to be addressed is the training of users. Radiation oncologists and residents will want to learn the physical basis for molecular imaging and how to use it in therapy. Similarly, there will be a demand from physicists for training in the interpretation, use, and quality assurance of molecular studies.

Molecular imaging in radiation oncology will represent a dramatic change in the way cancer is managed. At present, a chasm exists between what can be accomplished in the lab and what is actual routine diagnostic imaging practice in the clinic. The sophisticated image acquisition and processing techniques developed in the laboratory are not typically used in the clinic for various reasons, such as cost and difficulties related to implementation. Nevertheless, the presence of molecular images in therapy is increasing rapidly. The AAPM needs to be proactive in assisting a safe transition from research and development into routine clinical practice through the support of research, the dissemination of information, the training of physicists and oncologists, and the promulgation of guidelines for image acquisition, interpretation, and application.

Recommendations

The Ad Hoc Working Group recommends that the RTC form a Subcommittee for the emerging field of molecular imaging for clinical radiation oncology to educate the AAPM membership about this technology, to develop standards as needed, and to coordinate actions with other societies and the federal government. The application of molecular imaging technology to therapy is still in its infancy and, therefore, activities of the AAPM in this area will continue for at least 10-20 years. Given this timeframe, a permanent Subcommittee is recommended rather than an Ad Hoc subcommittee.

The Subcommittee should develop a set of recommendations, perhaps codified as standards, for the imaging process and for the application of the images to therapy. These standards should describe the physical and technical factors affecting image appearance and numerical accuracy and the procedures necessary to obtain images of suitable accuracy. They should describe the limitations of each modality with respect to radiotherapy planning and response assessment. They should define a nomenclature for using molecular images. This approach is similar to the way TG-51, for example, provides guidelines for absolute dosimetry techniques or the way that ICRU-50 and ICRU-62 standardize prescription and reporting of doses.

The Subcommittee should educate medical physicists through refresher courses and scientific sessions at AAPM, RSNA, and ASTRO annual meetings. It should publish educational and review articles and possibly editorials in medical physics related journals. It should assist medical physics training programs in adding education in molecular imaging.

Other professional societies, such as the Society of Nuclear Medicine, have an interest in how molecular images are used for therapy. For example, the number of submissions at the SNM annual meeting each year related to oncology is steadily increasing. The Subcommittee should develop and maintain liaisons with other scientific societies such as the SNM.

The Subcommittee should interact with NIH and other funding organizations to develop mechanisms to support basic and translational research in this field. It should assist governmental agencies when needed to assure that promulgated regulations are adequate, but not overly restrictive, and assist them in the establishment of appropriate reimbursements for molecular studies performed for therapeutic purposes.

Summary

In summary, the major goals of the Subcommittee should be to

- develop nomenclature for using molecular imaging in therapy,
- develop guidelines for producing molecular images appropriate for therapy,
- educate medical physicists on the imaging processes and their proper use in therapy,
- interact and coordinate with other professional societies,
- interact with NIH and other funding agencies to support research activities, and
- interact with government agencies regarding regulations and reimbursements.

The scope of work presented in this recommendation is too great for the Subcommittee to accomplish alone and so it is expected that the Subcommittee will recommend Task Groups to accomplish specific objectives or to focus on subspecialties within molecular imaging. The Subcommittee should monitor and review progress in this field and present its findings to the RTC in annual reports. Members of the Subcommittee should include representatives, as needed, from the Diagnostic X-Ray Imaging, Magnetic Resonance, Nuclear Medicine, and Research Committees.

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