LONG-TERM RECOMMENDATIONS

There will be a continuing interest and long-term benefits from the development of new instruments, probes, and related technologies to solve current problems and resolve important questions (eg, islet imaging).

The imaging information infrastructure must be in place to accommodate and effectively manage increasing amounts of diverse data, supported by the development of interchange standards for data and shared open-source software tools for analysis.

Networks of experts empowered with advanced unique instruments and methods will conduct scientific investigations by forming ad hoc multidisciplinary problem-solving teams – using support provided to build infrastructure BEFORE formulation of hypotheses. This extends the notion of glue grants a step further, in response to anticipated opportunities that emerge and attract the attention of expert teams without the impediment of incremental funding and at a pace out of sync with traditional funding cycles.

Assessment and Validation of Imaging Methods and Technologies

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Assessment and validation of imaging methods and technologies includes activities that range from early validation and technical assessment studies (generally conducted early in the development process) to large-scale, multi-institutional clinical outcome studies. The breakout session included individuals whose interests spanned the gamut of these activities. Discussion focused on summarizing the extent of the field, identifying challenges facing investigators and needs for the future, and formulating recommendations for specific initiatives which might advance the field. Additional thoughts regarding challenges and opportunities were also solicited from session attendees and are included in this summary.

OVERVIEW

The phrase "technology assessment" clearly has very different meanings to different individuals. Many in the group came to the breakout session interested primarily in the specifics of how new technologies are initially validated, specifically in issues related to how best to set parameters for acceptable precision/variability before moving forward with clinical trials. Others focused more on later-stage assessments, and were concerned more about supporting the development of an infrastructure to support large, rapidly conducted, multicenter clinical trials of new technologies. It was agreed that assessment and validation of imaging methods and technologies includes a continuum of activities. The group tried to include both ends of this continuum in its discussions and recommendations.

CHALLENGES AND NEEDS

The group identified a number of specific challenges facing investigators and needs for the future. At the most general level, it was agreed that needs could be divided into three types: 1) *Expertise* in study design and analytic methods; 2) *Infrastructure* to support the conduct of assessment studies, particularly large, later-stage clinical trials; and 3) *Funding* to support these activities and encourage investigators to participate. Furthermore, it was agreed that the availability of funding could facilitate the development of expertise and infrastructure. However, participants recognized that there is neither a sufficient number of appropriately qualified investigators, nor an adequate infrastructure to support the number and complexity of assessments that need to be conducted.

More specifically, the group recognized that there is a pressing need for the development of analytic methods specific to the assessment and validation of imaging methods and technologies, and that – if at all possible – every effort should be made to ensure that these analytic

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methods are widely disseminated as they are developed. Reference was made to the ROC analysis software developed by Charles Metz, which can be downloaded from the internet (http://www.bio.ri.ccf.org/Research/ROC/) and is widely used to conduct analysis of diagnostic test performance. However, it was felt that in most cases, analytic approaches and models developed by individual investigators generally remain proprietary and are not made available to others. In some cases, such as with a complex decision analytic disease model that took years to develop and might lead to a series of grants and/or publication, it was recognized that it would be unlikely that investigators would be willing to share their work. However, it was felt that in other cases, appropriate incentives could promote sharing of analytic approaches and models.

Beyond the specific challenges described above, perhaps the greatest challenge facing the field today is the need to effect a change in the culture of radiology. With respect to the session topic, it was felt that there is a great need to foster an appreciation of the value of participating in diagnostic technology assessments, and more generally, of the value of these studies. The group recognized that appropriate incentives (including better recognition by promotion committees) could help to effect this culture change, and that radiology could perhaps learn from other specialties, where greater exposure to academic activities in general, and clinical research in particular, is included as part of the residency and fellowship training experience. However, given the manpower shortage facing the field today and the economic realities facing many trainees, effecting a meaningful change in culture will be a difficult task.

RECOMMENDATIONS

The group identified a number of specific recommendations it felt could have an important effect on the field. These included: 1) that integration across the entire continuum of assessment and validation activities, and communication among the many participating disciplines, is essential; 2) that there is a need to support method development for all stages of assessment and validation activities; 3) that identification and validation of surrogate endpoints could help to improve assessment efforts and make trials more efficient; and 4) that modeling and simulation could have a very important role in diagnostic technology assessment.

Integration and communication are essential to make sure that appropriate methods are used at the appropriate stage in the assessment of each new technology. Ideally, validation studies in the lab should be conducted with an eye toward the eventual plan for animal and clinical assessment studies. By beginning to formulate tentative plans for later-stage assessments early in the development process, critical performance data can be accumulated early, and more efficient trials designed and conducted. Furthermore, organized surveillance and early engagement of promising new technologies can help target available resources for later-assessment studies to those candidate technologies likely to have the greatest impact on health outcomes.

As described above (Challenges and Needs section), there is considerable room for the development of analytic methods relevant to the assessment and validation of imaging technologies. The group recommended that resources be devoted to the development of biostatistical tools, approaches to understanding and incorporating the role of human observers in the assessment process, and the development of additional meaningful study endpoints. With respect to study endpoints, it was recognized that these must match the purpose of the study being conducted, but that they should ideally capture the effect of the imaging technology on patient outcomes such as length and quality of life.

Considerable discussion was devoted to the topic of surrogate endpoints. These are intermediate endpoints that have been validated as having a definite and predictable relationship with patient outcomes of concern. For example, reduction in tumor size or number of metastases, if shown to be predictive of patient survival or quality of life, could be useful surrogate endpoints for the evaluation of targeted therapies. The identification and validation of surrogate endpoints for a variety of diseases could help to expedite clinical trials, which could then be designed to capture data regarding the surrogate endpoints rather than patient outcomes that occur farther in the future.

The potential role and importance of modeling and simulation was also discussed. Modeling can help identify critical information to acquire in future trials. Modeling can be used to identify performance (or cost) targets that a new technology must meet to be an attractive alternative to existing technologies, or to identify critical information to acquire in future trials. Modeling can also be used to determine the effect of new technologies on patient outcomes based on shorter term, or surrogate, endpoints derived from clinical trials. In a modeling study, the short-term outcomes of concern (generally the probability of particular events) are defined in advance; the model is used to predict long-term outcomes and thus

extends available trial results. Existing trial results are then used to verify and calibrate the model, and model results can be used to refine the design of later trials. A modeling approach also offers more flexibility than randomized trials. For example, it is possible to compare more interventions and follow-up protocols than are practical in a trial. One can also simulate patient populations that did not participate in randomized trials, or evaluate potential improvements in test performance or advances in therapies. Lastly, the results of modeling studies are generally available more rapidly than clinical trials, and at a much lower cost.

ADDITIONAL THOUGHTS

A number of additional points were raised by the group. To begin with, it was recognized that education is absolutely essential if the field is to move forward. Clearly, there is a great need to educate trainees concerning the need and techniques for conducting rigorous assessments of imaging technologies. Better education of our trainees can also help to achieve the much needed "culture change" mentioned above. In addition, it is essential for radiologists and other imaging scientists to educate investigators working in other disciplines about the capabilities of imaging technologies, and the challenges we face in evaluating their performance. Reviewers, be they study section members or journal reviewers and editors, also need to be better educated regarding these issues. Finally, through ongoing dialog, it is critical to continue to raise the awareness of the National Institutes of Health and other funding agencies about the challenges and opportunities related to diagnostic imaging and its assessment.

The group also suggested that NIH extramural staff should make an effort to engage clinical investigators and imaging experts in the process of setting priorities for research funding and program development. Only by working together can the highest-priority issues be identified and addressed. In addition, it was felt that imaging scientists should make a greater effort to coordinate our research activities with investigators in other specialties so that research was focused on the topics of greatest clinical importance. All agreed that it is important that our research remain relevant to clinical problems.

Finally, the group agreed that industry, payers, and regulatory agencies were critical partners in the assessment and validation process. Industry and payers have important needs to understand the benefits and appropriate role of imaging technologies in medical care. They stand to benefit from the results of any assessment studies performed, and should share in the support of those studies. Regulatory and reimbursement agencies represent an important part of the overall process that ultimately controls the diffusion of new medical technologies (assessment is part of this process). It was felt that greater collaboration and transparency in these processes was needed. Specific examples offered included the need for regulatory agencies to work with investigators to validate and then accept surrogate endpoints, which would then be accepted by them in considering approval of new imaging technologies.

SUMMARY

In summary, the group identified many challenges and opportunities facing those wishing to conduct rigorous assessment and validation of imaging technologies. Specific needs and recommendations were outlined by the group. Overall, it was felt that the field has made great progress in the past several years, and that the future is promising.

Image-Guided Intervention

William R. Hendee, PhD, J. Daniel Bourland, PhD

The workshop described in this white paper occurred as part of a meeting on Biomedical Imaging Research Opportunities held in Bethesda, Maryland on January 31–February 1, 2003. The meeting was convened by the American Association of Physicists in Medicine (AAPM) and cosponsored by the Radiological Society of North America (RSNA), the Biomedical Engineering Society (BMES), and the Academy of Radiology Research (ARR). Thirteen other scientific organizations served as cooperating societies for the meeting.

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