Developing the RECIST Criteria Toolkit

NCCCP sites use this tool to improve compliance

In 2009 the NCCCP Best Practices Working Group of the Clinical Trials Subcommittee was tasked with developing a RECIST (Response Evaluation Criteria in Solid Tumors) criteria toolkit.

RECIST is a set of criteria defined by an international committee to measure tumor response via CT, MRI, and X-ray using formalized rules for measurement of tumor target lesions. While compliance with RECIST criteria in itself does not increase accrual to multi-modality clinical trials, the use of standard techniques and tools to measure response to treatment on imaging lends greater power and credibility to the results obtained, especially in multi-modality treatment plans. One of the goals of the Clinical Trials Subcommittee was to enhance NCCCP site compliance with use of the RECIST criteria in the evaluation of imaging studies used to measure response to treatment of solid tumors. As part of this effort, educational materials and tools were provided to physicians and clinical trial professionals within the network. The resources were designed to simplify the process of measuring and comparing time imaged malignant lesions across studies. NCCCP sites were able to use the tools for education, adoption, and/or implementation as they deemed appropriate.

Historical Background

RECIST criteria were initially published in 2000 in the *Journal of the National Cancer Institute* and subsequently revised in January 2009 (RECIST 1.1) in the *European Journal of Cancer.* Though RECIST is largely known in terms of measurement guidelines, the RECIST criteria also address issues related to different imaging technologies such as PET, MRI, CT, with and without contrast, as well as lesions in bone or those with cavitation. While RECIST criteria are internationally accepted, they are not mandatory and are not an NCI standard. Salient features of the changes in the RECIST criteria include:

1. Decrease of maximum target lesions from 10 to 5 total and from 5 to 2 per organ.
2. Disease progression requires both a 20 percent increase in tumor size AND a 5 mm absolute increase.
3. Information has been added regarding the use of PET/CT scanning and other imaging in the detection of new lesions.
4. For the measurement of lymph nodes, the short axis is to be measured and the axis must be ≥ 15 mm to be considered measurable.

Toolkit Development

Many NCCCP sites collaborated in the development of the RECIST toolkit. Through monthly conference calls and the sharing of experiences within each institution's research community, the basic goals and needs for this program were assessed. Many institutions provided previously utilized measurement flowsheets, while others provided PowerPoint presentations already in existence at their institutions. NCCCP sites with early success in integrating RECIST measurements consistently into their SOPs shared their experiences and best practices. In addition, a PowerPoint presentation provided an overview of RECIST specifics and a rationale that could be shared with radiology staff.

The RECIST toolkit provides templates for the reporting of data and source documentation for sponsor and cooperative group audits, and simplifies monitoring of disease for response. RECIST toolkit components are organized in two categories: NCCCP-generated documents and reference documents.

NCCCP-generated RECIST toolkit documents include:

- Introduction to the "Toolkit"
- Template guideline and a sample standard operating procedure (SOP)
- Summary and quick reference document
- Tumor measurement summary template
- Implementation matrix.

Reference documents in the RECIST toolkit include:

- Original *JNCI* article on RECIST from 2000.
- Updated *European Journal of Cancer* article from 2009
- PowerPoint presentation by Stephen S. Grubbs, MD, Christiana Care, Del. dated 2005. (This presentation does *not* reflect 2009 changes.)
- PowerPoint presentation by EORTC regarding the RECIST 1.1 changes.

Toolkit Implementation

As all NCCCP clinical sites have different constituencies, how each site approaches the process of optimizing the recording of necessary data is best left to the individual institution. NCCCP sites offer these considerations to other community cancer centers looking to enhance compliance with RECIST criteria:

1. Have a designated radiologist or team of radiologists assigned to RECIST compliant readings. (Availability of picture archiving and communication system [PACS] technology is helpful.)
2. Use Grand Rounds and educational venues for this type of presentation to radiologists to emphasize importance of RECIST.
3. Use a summary of RECIST readings signed by a radiologist or PI (principal investigator) to facilitate source documentation.
4. Budget appropriately in industry trials to account for

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the additional RECIST workload. (This option is not available in Cooperative Group trials.)

Success in implementing the RECIST toolkit required the buy-in of radiologists and radiology technicians, medical and radiation oncologists, and the clinical research team. The NCCCP PI was essential to help drive the implementation process. NCCCP sites found two toolkit components most useful: 1) the tumor-size measurement flowsheet, which enhanced consistency of measurement from scan to scan, and 2) the quick-reference guide for physicians.

The implementation process created an opportunity to discuss and more fully appreciate the constraints on both the researchers and the radiologists. Many of the radiologists became aware of the specificity by which clinical trials determine improvement or progression, while the clinical research team became more aware of the manpower constraints within the radiology department that made it difficult for the radiologists to comply with requests. Some NCCCP sites created a process of identifying clinical trial patients on requisitions, which generally resulted in more attention to RECIST criteria in these highlighted patients. In addition, having an interdepartmental team seemed to help improve communication and process development across departments within an institution.

NCCCP sites continue to evaluate the overall experience in rolling out the RECIST toolkit. The project requires significant time investment to develop and implement the processes involved and to garner support from the stakeholders. Because this project increases the work and time involved for a radiologist to interpret a diagnostic study, ongoing reinforcement about the project's importance is key.

Barriers and Challenges

While many NCCCP sites are in the process of implementing and fine-tuning the process, other sites face a few predictable barriers. For example, implementation of the RECIST toolkit requires a change in workflow for secretaries, schedulers, physicians who need to identify clinical trial patients on requisitions, and—most importantly—for the radiologists who have not incorporated RECIST evaluation in routine radiology practice. Many of the institutions deal with large hospital-based and/or private practice radiology groups with multiple offices, making it difficult to isolate a core group of radiologists to function as the RECIST "team." This barrier introduces an added level of institutional inconsistency that detracts from the goals of the project and accountability. However, with the digitization of films and PACS technology, identifying a designated group of radiologists for the research process can be improved.

NCCCP sites with multidisciplinary teams and integrated radiologists found it easier to have a consistent radiologist involved in the process to facilitate the successful

Case Study

Concurrent with the NCCCP's decision to move forward with a RECIST education and implementation program, research staff at one NCCCP site were noting inconsistencies in measurement and tracking of reference lesions. A subsequent audit by a cooperative group confirmed the concerns raised by the research staff. Rather than "reinventing the wheel," this site was able to share and learn from other NCCCP site experiences with similar issues and the processes used to correct them.

The site works with a 30+ member radiology department located in various sites of service. The patients on research trials use multiple facilities to obtain radiographs, so a process was needed to disseminate this information to the radiologists staffing these locations. Having one radiologist do all the reviewing for RECIST was not feasible. However, researchers identified one radiologist who became their advocate and agreed to present the details of RECIST at the equivalent of radiology Grand Rounds. While this NCCCP site did not anticipate universal acceptance of the required changes, the site hoped to achieve sufficient "buy-in" to create a RECIST core group.

PACS availability allows this core group to review films performed in other locations without much difficulty. In addition, physicians have received a tumor measurement flowsheet created by the NCCCP for assistance in identifying what is measurable and to show the history of the lesions' measurements.

Secretaries and research physicians had to be trained to somehow identify a patient in a clinical trial to allow for "special handling" of each case.

Research staff now has a better appreciation of how these efforts affect radiology workflow and have been more aggressive in funding a radiology line item in studies in which there is a budget. In most other studies, the radiologists' efforts—the extra time and effort it takes to be in compliance with RECIST criteria—have largely been uncompensated.

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implementation of RECIST within their department and/or program.

Metrics

One NCCCP site led the effort to create a matrix tool that network community cancer centers could use to quantify their RECIST implementation status and monitor progress quantitatively.

Fifteen of the 16 NCCCP sites implemented RECIST and were able to compare their performance on the assessment tool pre-intervention to post-intervention. Here's what the matrix data revealed:

- All participating sites saw an increase in average score from baseline of 8.9 to 13.
- Sites were able to make the most progress around the education and coordination measures, with an average score increase of 2.6 for all sites in those two areas.
- Ten sites demonstrated progress from baseline, revealing that many sites benefited from this best practice project.
- Four sites that did not have a process at baseline (scores of 1 in all categories) were able to make significant progress with scores, averaging a 10 point improvement increase.
- Four sites that scored above 6 (entry score) did not make any additional progress.
- One site scored 21 and was able to provide expertise and support in the development of this project.
- The site that demonstrated the greatest benefit from the project saw a 13 point score increase. Analysis of interventions performed at this site will hopefully help other sites fine tune their processes.
- While a score of 30 is best practice; the highest score among the NCCCP sites was 22. This finding clearly shows that this process is difficult, requiring coordination and commitment to accomplish the best practice outcome.

The data demonstrated the clear success of sharing best practices across NCCCP sites and of learning from a site that was performing at a significantly higher level. New users of the matrix and the sites that did not make significant progress along the matrix need to consider how best to implement the RECIST matrix into their clinical trial program.

Overall, participating sites viewed the process of developing and implementing the RECIST program as a positive experience. The development process was collaborative since all sites had dealt with this problem in one form or another. The conference calls provided an opportunity to discuss what each site had learned from prior interventions on this issue.

Although it is too early to assess the full extent of the RECIST toolkit success, it is evident that talking about the process created a level of dialogue between the involved disciplines that had not always existed previously and allowed for a better understanding of the logistical issues at each institution. The most often-cited recommendation from participating sites was to have a physician "champion" within the radiology group who could help spearhead the process rather than having the initiative appear to be something imposed by an outside entity.

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