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Quantitative Imaging in Oncology Patients: Part 2, Oncologists' Opinions and Expectations at Major U.S. Cancer Centers

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OBJECTIVE. The purpose of this article is to examine oncologists' opinions and expectations concerning imaging and tumor measurements in patients with cancer.

MATERIALS AND METHODS. An electronic mail survey was sent to 2,400 medical, gynecologic, and radiation oncologists at 55 U.S. National Cancer Institute–funded cancer centers. The survey contained questions about departmental demographics, opinions regarding imaging for patients with cancer, PET/CT utilization, and utilization of the Response Evaluation Criteria in Solid Tumors (RECIST) system in therapy protocols that use imaging as a therapeutic end point.

RESULTS. A total of 492 responses (21%) were received. Sixty percent (294) of respondents were medical oncologists, 9% (45) were gynecologic oncologists, 26% (127) were radiation oncologists, and 5% (25) answered "Other." Ninety-eight percent (431/438) of respondents provide clinical care, and 99% (420/425) have participated in clinical trials. Most respondents (94% [410/438]) expect some or all tumors to be measured at the time of standard initial clinical imaging. Over half (65% [275/426]) think that tumor measurements should be bidimensional. Only 25% (101/400) of respondents' institutions have department rules on the implementation of RECIST measurements. Sixty-eight percent of participants (269/397) think that RECIST is flawed but serviceable. Over half of respondents (56% [221/398]) were not familiar with RECIST 1.1 modifications.

CONCLUSION. Most oncologists at National Cancer Institute–sponsored cancer centers expect tumor measurements to be made in the routine imaging of patients with cancer. Almost two thirds of respondents think that bidimensional measurements of index lesions are satisfactory in routine oncologic imaging. Little consensus exists in the implementation of RECIST measurements for clinical trials at these centers.

Keywords: oncologist, RECIST, tumor measurements

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Evidence-based medicine, which has been defined as the "conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients" [1], has become one of the guiding principles of patient care in the 21st century. Clinicians assemble available data to assess and alter therapy, and imaging often plays a central role in this complex decision process. With the shift toward evidence-based medicine, there is an expectation for quantitative image interpretation, and oncology is one arena where quantitative image is perceived to have an important impact. Imaging-derived tumor measurements are routinely used as a biomarker—that is, a testable end point indicative of a relevant biologic aspect of cancer [2]. Tumor measurements are used to monitor disease response in pharmaceutical trials by providing evidence of either progression or response to therapy, and it is widely hoped that the early prediction of drug efficacy can shorten the length of and, subsequently, the cost of a clinical trial [3–5]. Requirements for quantitative tumor metrics in oncologic pharmaceutical trials have led oncologists to become frustrated with qualitative interpretations by radiologists [6]. Our results from another survey [7] suggest that radiologists in major cancer centers have adapted their interpretations to satisfy oncologists' increasing demands for quantitative imaging. Questions remain, however, about the uniformity or range of oncologists' expectations and whether radiologists are meeting those expectations.

Although there is an abundance of data documenting the usefulness of tumor measurements in clinical trials, there are few data about

oncologists' perceptions of or expectations for the radiologist's role in oncologic imaging. Having recently completed a survey of radiologists regarding oncologic imaging [7], we were interested in balancing the radiologists' perception of oncologic imaging with a survey of oncologists' expectations. To our knowledge, there have been no studies querying oncologists' expectations about quantitative measurements on imaging studies. In this study, our aim was to examine oncologists' opinions regarding oncologic imaging interpretations.

Materials and Methods

A 45-question survey (Appendix 1) was sent to 2,400 oncologists at the 55 U.S. National Cancer Institute–funded cancer centers. Recipients were informed that their responses would be anonymous. These medical, gynecologic, and radiation oncologists were identified from their cancer centers' Web pages, and those with publicly accessible e-mail addressees were contacted. The survey was sent via electronic mail using an online survey program (Survey Monkey). The survey was sent three times to maximize the response rate.

The survey included "single-best-answer" questions as well as "choose from the following" and "select all that apply" questions. Only the first question required an answer; all other questions did not require an answer for completion of the survey. Our institutional review board does not require approval for this type of study. All recipients of the survey were informed of the purpose of this study.

Demographics

The recipients of the survey were first asked about their branch of oncology (medical, gynecologic, or radiation). Those who answered "none of the above" were excluded from the survey. Respondents were asked to select all applicable subspecialties by malignancy (e.g., breast or melanoma). They were queried about hospital size, hospital type of practice (academic or teaching, private practice with some residencies, or private practice with no residencies), oncology division size, and their typical amount of clinical contact with patients. We did not ask respondents for identifying information, nor did we ask for age or sex.

New Patient Workup and Imaging

Survey recipients were asked whether they requested that prior outside imaging studies be brought to the first patient visit for addition to their local image archive (PACS). Recipients were queried about the radiology department's willingness to interpret outside imaging. The oncologists were asked about their expectations for tumor measurements in the interpretation of the initial CT examination—that is, all tumors measured, some measured, the primary lesion measured with general descriptions of metastases, or Response Evaluation Criteria in Solid Tumors (RECIST) rules followed. Survey recipients were then queried about their expectations for tumor metrics in follow-up scans (answers included all tumors measured and compared, index lesions noted on prior scans measured and compared, new index lesions measured, and only qualitative description necessary).

Recipients were asked whether, in a situation where no tumor measurement was reported, they requested an addendum to the radiology report. Subjects were asked whether the radiologist should report tumor measurements routinely in patients with cancer who are not enrolled in a clinical trial and what the appropriate number of tumor measurements should be in a patient with metastatic disease.

The Use of PET/CT in Patients With Cancer

The oncologists were asked whether it was clear to them which malignancies are best evaluated with PET/CT. Recipients were then asked whether there was a subset of patients for whom they preferentially ordered PET/CT over CT alone (e.g., breast cancer, lung cancer, or melanoma) and whether they expected the same tumor measurements with PET/CT that they receive with CT reports. Recipients were asked whether they were familiar with the National Oncologic PET Registry. The oncologists were queried about PET/CT protocols and whether IV contrast material was requested. Finally, the recipients were asked whether they expect the same type of tumor measurements in PET/CT reports that they get in CT reports.

Unexpected Findings in Patients With Cancer

Recipients were asked whether they think it is the radiologist's responsibility to contact them with unexpected findings. They were then asked to select from a list of clinical scenarios those that required notification. The list included the following: acute process requiring immediate medical attention, contrast reaction or extravasation, marked progression of disease, and an incidental finding requiring long-term follow-up.

Opinions on Tumor Measurements in Oncologic Imaging

Recipients were asked a series of questions reflecting opinions about tumor measurements in oncologic imaging and were asked to select "agree" or "disagree" or select from a variety of options. These included whether dictation of all tumor measurements in routine clinical interpretations is the responsibility of the dictating radiologist; whether dictation of tumor measurements for several index lesions on routine clinical interpretations is satisfactory to document disease response or progression in routine oncologic imaging; whether a comment on increase or decrease in tumor size without measurements is sufficient to document disease response on routine clinical interpretations; whether tumor measurements should be bidimensional or unidimensional; whether patient management is affected by providing tumor measurements; and whether patient management is impeded by the absence of tumor measurements. Recipients were asked whether it is most advantageous to obtain measurements based on the index lesions identified on the first study (regardless of interval change), on index lesions identified on the most recent comparison, or on index lesions showing the most interval change since the comparison.

Oncologic Imaging and Response Evaluation Criteria in Solid Tumors

Recipients were asked whether an institutional committee, division, or department had rules on how RECIST measurements should be handled (e.g., who to contact within radiology or whether there are fixed charges for RECIST measurements) and whether there was an organized process for performing RECIST measurements in oncologic protocols. They were asked whether funding was provided for the person performing RECIST measurements and whether radiologists performing measurements had been included in academic manuscripts as coauthors on the basis of the performance of measurements.

Subjects were asked whether they were able to distinguish between target and nontarget lesions on the basis of RECIST guidelines, whether they were familiar with recent modifications to the RECIST criteria (RECIST version 1.1, Perceptive Informatics), and whether they thought that the reduction in the number of target lesions in RECIST 1.1 reduces accuracy in determining disease response. Recipients were asked whether, in their experience, an increase in target lesion size or development of new lesions was a more common cause of disease progression. The oncologists were then asked to categorize their experience with RECIST (i.e., very helpful; flawed, but serviceable; or flawed, and not useful for clinical management of patients).

Approval Process for Industry-Sponsored Oncology Trials With Imaging-Determined End Points

Recipients were asked whether they participated in oncologic therapy trials. Those who had participated were asked whether they had been a principal investigator and whether, if imaging is a therapeutic end point, they are required to ob-

TABLE 1: Oncologists' Clinical Specialties

Specialty	No. (%) of Respondents (*n* = 450)
Head and neck	46 (10)
Genitourinary	232 (52)
Breast	122 (27)
Gastrointestinal	118 (26)
Pancreas	98 (22)
Liver and biliary	71 (16)
Lung	118 (26)
Gynecologic	78 (18)
Melanoma	44 (10)
Sarcoma	75 (17)
Lymphoma	106 (24)
Other	44 (10)

tain approval by the radiology department before initiating a trial. Respondents were asked whether they had a specific person in the radiology department to contact regarding imaging protocol approval before initiating an oncologic therapy trial and whether there was a radiology committee through which budget approval had to be obtained before initiating an oncologic therapy trial if imaging was a therapeutic end point. Recipients were asked whether they had drafted budgets and were asked to list the components of the radiology budget included in their therapy trials (i.e., funding for scan acquisition, image archiving, image interpretation, RECIST measurements, or other).

Statistical Analysis

The data were collected and tabulated by the online survey program. Readers may approximate the standard error of percentages given by using the following formula: standard error in percentage = $100 \times \sqrt{p(1-p)/n}$, where p is the proportion of respondents with a characteristic and n is the unweighted number of respondents [8].

Results

Respondent Demographics

Four hundred ninety-two responses (21%) were received. None of the respondents answered every question in the survey. Sixty percent (294/491) of respondents were medical oncologists, 9% (45/491) were gynecologic oncologists, and 26% (127/491) were radiation oncologists. Five percent (25/491) answered "none of the above" and were excluded from further analysis. Eighty-four percent (248/294) of medical oncologists answered all 45 questions, as did 89% (40/45) of gynecologic oncologists and 80% (102/127) of radiation oncologists. Hospitals ranged widely in size, with 31% (136/445) of respondents affiliated with hospitals with 501–750 beds, 26% (117/445) affiliated with hospitals with 201–500 beds, 25% (112/445) affiliated with hospitals with 751–1,000 beds, and 9% affiliated with hospitals with 0–200 and > 1,000 beds (38/445 and 42/445, respectively). Most respondents were from academic teaching hospitals (96% [431/448]). Oncology divisions also varied widely in size, but were most commonly greater than 20 physicians (42% [190/449]). Thirty-two percent (145/449) ranged from one to 10 oncologists, and 25% (114/449) included 11–20 oncologists. Nearly all respondents (98% [431/438]) routinely saw patients in clinical practice. The amount of time allocated to clinical patient care varied considerably, most commonly 61–80% (29% [130/449]), with 25% (113/449) of respondents describing their work as 41–60% clinical and 21% (92/449) describing their work as 81–100% clinical. Clinical specialties spanned a variety of malignancies (Table 1), most commonly genitourinary (52% [232/450]), breast (25% [112/450]), gastrointestinal (26% [118/450]), and lung cancer (26% [118/450]).

New Patient Workup and Imaging

Most (78% [341/438]) respondents request that new patients bring prior images to their first visit for subsequent archiving in PACS. Only 1% (6/438) never request prior images. Thirty-nine percent (171/438) of respondents receive formal interpretations of outside images, whereas 37% (160/438) are offered an opinion from a radiologist without a formal interpretation. A small number (11% [47/438]) of radiology departments will not interpret outside images.

Expectations for interpretation of the initial CT examination for patients in the oncology department varied, with 31% (137/438) of oncologists thinking that all tumors should be described and measured and that image numbers should be recorded. Thirty percent (133/438) expect that some representative tumors should be described and measured and that image (e.g., slice) numbers should be recorded, and 21% (91/438) think that the primary tumor should be measured with metastatic lesions described in general terms. Eleven percent (49/438) of respondents expect RECIST guidelines to be followed for target and nontarget lesions. Six percent (28/438) of respondents answered "I don't know" or "Other." Oncologists' opinions regarding tumor measurements are broken down by subspecialty in Table 2.

When follow-up CT scans are obtained, 47% (204/438) of responding oncologists expect that all tumors should be measured and compared with prior scans. Thirty-four percent (149/438) of respondents think that tumor measurements can be limited to index lesions noted on the original study, whereas 9% (39/438) would accept limiting tumor measurements to several index tumor lesions (but not necessarily the same lesions that were previously measured). Three percent (11/438) of oncologists think that tumors can be described in general terms (increasing or decreasing), without the inclusion of measurements, and 8% (34/438) replied "Other." If tumor measurements are not included in the original interpretation, 83% (362/436) of respondents would request an addendum with measurements.

Half (216/436) of the respondents think that tumor measurements in patients receiving routine oncologic regimens should match those required for patients enrolled in a clinical trial. Forty three percent (188/436) of respondents think that measurements in this situation should be routinely performed but are not as concerned about the number of lesions measured. Five percent (22/436) of respondents think tumor measurements do not need to be reported routinely in patients with cancer who are not enrolled in a clinical trial.

When asked about the appropriate number of lesions measured per organ in a patient with metastatic disease, 40% (172/434) of respondents expressed no preference. Other responses included two lesions per organ (27% [118/434]), five lesions per organ (18% [76/434]), "I don't know" (12% [54/434]), and one lesion per organ (3% [14/434]).

The Use of PET/CT in Patients With Cancer

When asked whether it was clear to them which malignancies are best evaluated with PET/CT, 55% (240/434) of respondents answered yes, although the radiation oncologists were more confident (68%) than their medical or gynecologic counterparts (50% and 51%, respectively). Oncologists preferentially order PET/CT across a broad variety of malignancies (Table 3), but the most common cancers listed were lung cancer (48% [184/382]), lymphoma (23% [87/382]), and gynecologic cancer (20% [76/382]), closely followed by breast cancer (18%), head and neck cancer (17%), and melanoma (16%). The majority (60% [258/431]) of respondents were familiar with the National Oncologic PET Registry.

TABLE 2: Oncologists' Opinions on Tumor Measurements, by Specialty

Question, Answers	Medical Oncologist	Gynecologic Oncologist	Radiation Oncologist
Expectation for interpretation of initial CT examination			
All tumors measured	73/279 (26)	18/43 (42)	46/115 (40)
Representative tumors measured	116/279 (41)	5/43 (12)	14/115 (12)
Primary tumor measured with metastatic lesions described in general terms	41/279 (14)	10/43 (23)	41/115 (36)
Follow RECIST for target and nontarget lesions	31/279 (11)	10/43 (23)	8/115 (7)
I don't know	1/279 (< 1)	1/43 (2)	1/115 (1)
Other	17/279 (6)	3/43 (7)	5/115 (4)
Expectation for interpretation of follow-up CT scans			
All tumors measured	114/279 (41)	27/43 (63)	63/115 (55)
Representative tumors measured	112/279 (40)	7/43 (16)	29/115 (25)
Primary tumor measured with metastatic lesions described in general terms	20/279 (7)	4/43 (9)	15/115 (13)
Follow RECIST for target and nontarget lesions	6/279 (2)	1/43 (2)	4/115 (3)
I don't know	1/279 (< 1)	0	0
Other	26/279 (9)	4/43 (9)	4/115 (3)
Appropriate no. of lesions measured per organ in patient with metastatic disease			
1 per organ	4/279 (1)	1/43 (2)	9/111 (8)
2 per organ	83/279 (30)	8/43 (19)	27/111 (24)
5 per organ	62/279 (22)	3/43 (7)	11/111 (10)
I don't have a preference	100/279(36)	25/43 (58)	46/111 (41)
I don't know	30/279 (11)	6/43 (14)	18/111 (16)
Most common cause of disease progression according to RECIST criteria			
Increase in target lesion size	152/248 (61)	26/41 (63)	9/106 (8)
Development of new lesion	73/248 (29)	13/41 (32)	57/106 (54)
I don't know	9/248 (4)	23/41 (56)	16/106 (15)

Note—Data are no. of respondents/total (%). The denominators are not all the same because respondents were not required to answer all questions in the survey.
RECIST = Response Evaluation Criteria in Solid Tumors.

A small majority of respondents (53% [227/431]) expect the same type of tumor measurements in PET/CT reports as in CT reports, with breakdown by specialty as follows: medical oncologists, 50% (136/274); gynecologic oncologists, 54% (23/43); and radiation oncologists, 60% (67/113). Thirty-eight percent (166/435) of oncologists order PET/CT with IV contrast material most of the time (depending on malignancy), with 12% (54/435) requesting contrast material a minority of the time (depending on malignancy). Only 2% (10/435) of respondents do not order IV contrast material. More than a third (38% [163/435]) of respondents report that their institution does not use IV contrast material for PET/CT. Six percent (25/435) did not know whether they request IV contrast material, and 4% (17/435) do not order PET/CT.

Unexpected Findings in Patients With Cancer

Most respondents (92% [400/435]) think that it is the radiologist's responsibility to contact clinicians with unexpected findings, whereas 6% (26/435) disagree and 2% (9/435) did not know. Nearly all respondents (99% [432/435]) expect notification for an acute process requiring immediate medical attention (e.g., deep venous thrombosis). Fifty-nine percent (256/435) of respondents expect notification in cases of contrast reaction or extravasation. Forty-six percent (201/435) of respondents would like to be notified in cases of marked progression of disease. A small number (18% [80/435]) of respondents expect notification for an incidental finding requiring long-term follow-up (such as a small pulmonary nodule). Five percent of those surveyed (21/435) selected "Other."

Opinions on Tumor Measurements in Oncologic Imaging

The majority of responding oncologists think that the inclusion of tumor measurements in routine clinical interpretations is the responsibility of the dictating radiologist (64% [272/424]). A large majority (91% [385/424]) of respondents consider dictation of tumor measurements for several index lesions on routine clinical interpretations satisfactory to document disease response or progression in routine oncologic imaging. Seventy percent (299/426) of respondents think that an interpretation that describes an increase or decrease in tumor size without measurements is not sufficient to document disease response. Tumor measurements should be bidimensional according to a majority (65% [275/426]) of respondents. Twenty-eight percent (118/426) of respondents are indifferent to the method of tumor measurements as long as the technique is consistent, and 8% (32/426) favor unidimensional measurement.

The vast majority (93% [397/425]) of respondents think that patient management is affected by the inclusion of tumor measurements in radiologic interpretations. Most (78% [334/426]) respondents think that the radiologist impedes patient management by

TABLE 3: Oncologists' Preference for PET/CT Over CT Alone, by Specialty

Specialty	No. (%) of Respondents (*n* = 382)
Head and neck	66 (17)
Genitourinary	17 (4)
Breast	68 (18)
Gastrointestinal	55 (14)
Pancreas	44 (12)
Liver and biliary	13 (3)
Lung	184 (48)
Gynecologic	76 (20)
Melanoma	61 (16)
Sarcoma	34 (9)
Lymphoma and leukemia	88 (23)

Note—Fifty-one respondents (13%) stated that they do not use PET/CT.

omitting tumor measurements. When monitoring tumor growth, 37% (156/419) of respondents preferred measurements based on lesions identified on the most recent comparison, whereas 32% (132/419) preferred measurements of index lesions showing the most significant change in size since the comparison, and 24% (101/419) preferred measurements based on index lesions identified in the first study, regardless of interval change.

Oncologic Imaging and Response Evaluation Criteria in Solid Tumors

When asked whether an institutional committee, division, or department had rules on how RECIST measurements should be handled, 38% (150/400) did not know, 37% (149/400) answered "no," and 25% (101/400) replied "yes." Forty-two percent (166/399) of respondents noted that the implementation of RECIST measurement in oncologic protocols was an ad hoc issue for the radiology department with each new oncologic trial protocol undertaken, only 10% (39/399) have a committee for approval of RECIST measurements, and 8% (33/399) approach the same individual radiologist each time for RECIST measurements. Forty-six percent (182/397) of respondents did not know whether funding was provided for the person performing RECIST measurements, and 40% (159/397) stated that no funding is provided. When asked whether radiologists performing RECIST measurements had been included in academic manuscripts as coauthors on the basis of this contribution to the trial, 33% (130/392) of respondents answered "yes," 29% (114/392) replied "no," and 38% (148/392) did not know.

A large majority of respondents (81% [323/398]) were able to distinguish between target and nontarget lesions on the basis of RECIST criteria. Fifty-three percent (211/396) of respondents think that the most common cause of disease progression is an increase in target lesion size, whereas 36% (143/396) think progression of disease is most commonly secondary to a development of a new lesion. Fourteen percent (54/397) of respondents think that RECIST is "very helpful," 68% (269/397) think that it is "flawed, but serviceable," 5% (21/397) think that it is "flawed, and not useful for clinical management of patients," and 13% (54/397) do not know.

A small majority (56% [221/398]) of respondents was not familiar with recent modifications to the RECIST criteria (RECIST version 1.1). Only 13% (50/397) of respondents think that the reduction in the number of target lesions in RECIST 1.1 will reduce accuracy in determining disease response.

Approval Process for Industry-Sponsored Oncology Trials With Imaging-Determined End Points

Nearly all respondents (99% [420/425]) participate in oncologic therapy trials, with 81% (336/413) of those involved having served as a principal investigator in an oncologic therapy trial. Fifty-eight percent (239/412) of respondents are required to obtain imaging protocol approval from the radiology department before initiating an oncologic therapy trial if imaging is a therapeutic end point, although only 38% (154/411) have a specific radiology contact regarding imaging protocol approval. When asked whether budget approval had to be obtained from a radiology committee before initiating this type of oncologic therapy trial, similar percentages of respondents answered "no" (39% [159/411]) or "I don't know" (38% [156/411]), with only 23% (96/411) answering "yes."

Most respondents (71% [291/413]) had experience in creating budgets. Respondents were asked to select from a list of items included in the radiology portions of their oncology trial budgets and were able to select all that applied. The most common radiology component of a trial budget was funding for scan acquisition (55% [215/394]), followed by image interpretation (44% [175/394]), RECIST measurement (24% [93/394]), and image archiving (19% [76/394]). Eight percent (30/394) replied "Other," with 11 of these replies (3% of total respondents) stating that imaging funding is provided only if the imaging falls outside the standard of care for follow-up.

Discussion

Although qualitative radiologic diagnosis represents a large part of the practice of clinical radiology at this time, the integration of evidence-based medicine into daily patient care has driven and will continue to drive expectations for quantitative results in imaging. Oncologic imaging is one of the areas at the forefront of quantitative imaging because tumor measurements are used as a biomarker to evaluate cancer progression or response to therapeutic agents. In addition, it has been suggested that an emphasis on quantitative imaging is critical to support adaptive trial design [9]. To date, there have been no studies investigating the oncologists' perspectives on quantitative imaging in their patient population. The purpose of this study was to examine the opinions of oncologists with regard to the role of quantitative measurements in oncologic imaging.

We chose to define our survey audience as all medical, gynecologic, and radiation oncologists practicing at cancer centers with National Cancer Institute sponsorships to sample the oncologist population familiar with pharmaceutical trials and RECIST measurements. We designed our survey to allow respondents the option of answering each question individually. The first question was designed to limit our respondent population to the aforementioned oncology groups. To decrease frustration, no other questions required an answer to proceed. Our response rate of 21%, although lower than the corresponding survey of radiologists' opinions [7], is in line with published response rates from online surveys [10–13].

The majority (93%) of our survey respondents think that tumor measurements are important for patient management, and 78% think that patient management is adversely affected when radiologists omit tumor measurements. One third of respondents think that all tumors should be described and measured on the initial interpretation, and almost half of respondents think that all tumors should be measured on follow-up imaging and compared with previous scans. These expectations are above and beyond that of RECIST 1.0 and 1.1 guidelines and are at odds with the current practice patterns of most abdominal radiologists, of which only 7% and 2% dictate all tumor measurements on the initial scan and follow-up imag-

ing, respectively [7]. The inclusion of all tumor measurements in clinical interpretations would be an overwhelming burden to the radiology clinical workload, because many centers scan hundreds of patients each day for oncologic indications. The discrepancy between oncologists' expectations and radiologists' practices highlights one of the many areas of controversy found in the practice of oncologic radiology. Many questions regarding the role of the radiologist in oncologic imaging exist: what should be the standard of care for the clinical interpretation when a patient is involved in a clinical trial, should there be a difference in clinical interpretations for patients who are enrolled in pharmaceutical trials versus those who are not, and should the radiologist providing the clinical interpretation include measurements for the RECIST target lesions in the clinical report? Half of the oncologist respondents think that tumor measurements in patients on routine oncologic regimens should match those required for trial patients. In many institutions, one radiologist provides the clinical interpretation (for patients enrolled in a clinical trial) and another provides the RECIST measurements [7]. Coordinating the inclusion of the target lesion measurements in the clinical "read" is a difficult challenge. Although the oncologists believe strongly that these efforts should be synchronized seamlessly, the practice of oncologic radiology is not meeting the challenge at the current time.

More than half of the respondents considered themselves well informed on the appropriate utilization of PET/CT in the evaluation of malignancies, and most were familiar with National Oncologic PET Registry. The choices of which malignancies to image with PET/CT (lung cancer, lymphoma, gynecologic malignancies, breast cancer, head and neck cancers, and melanoma) are similar to those reported in the literature [14–16]. The use of IV contrast material in PET/CT was variable, and this controversy is similarly evident in the literature [17–20]. Just over half of the respondents expect similar tumor metrics in PET/CT reporting. Although the optimal role for FDG PET in clinical oncology is still evolving [21], there is increasing endorsement for image quantification in these studies, including tumor size from the CT scan and relative tracer uptake as measured with the standardized uptake value from the PET scan. There is ongoing work to establish techniques for reducing bias and variance in quantitative PET/CT results for monitoring response in clinical practice and clinical trials [22].

More than two thirds of the respondents think that description of an increase or decrease in lesion size without tumor measurements is not sufficient to document disease response. This opinion is similar to that of the surveyed abdominal imagers at the corresponding institutions (61%) [7]. More than half of the respondents prefer bidimensional tumor measurements. These results suggest that oncologists expect more than the criteria established by RECIST, where measurements are unidimensional. This expectation is, in fact, concordant with what is generally being provided by radiologists. According to our recent survey of radiologists, 86% of respondents dictate bidimensional measurements [7].

Most respondents were familiar with RECIST criteria; however, over 50% were not aware of the changes implemented in RECIST 1.1 [23]. This lack of awareness may reflect the fact that changes to RECIST guidelines were implemented in early 2009 and most ongoing protocols still used RECIST 1.0 at the time of this survey. The majority of respondents think that RECIST is "flawed but serviceable." More than half of the respondents think that the most common radiologic indicator of disease progression is an increase in target lesion size. However, a recent review of a large number of cases comparing the RECIST 1.0 and RECIST 1.1 criteria by the RECIST Working Party [24] found that the majority of cases classified as progressions by imaging criteria were categorized as such because of the appearance of a new lesion on an imaging study, with or without growth of target lesions.

Almost all of the respondents had participated in oncologic therapy trials, and many had served as principal investigator on one of these studies. Just over half of the respondents said that if imaging is a therapeutic end point, then their institution required approval of the imaging component of a clinical trial protocol before initiating an oncologic therapy trial. The approval process and budgeting for the imaging portion of the study are highly variable because most of the respondents either did not allot funding for the imaging portion of the trial or did not know whether there was funding available for this component. Implementation and funding of RECIST measurements in these oncologic trials are also variable. This finding suggests that, from the oncologists' perspective, funding for the implementation of imaging in these trials are either not needed or not a high priority in budget development. The National Cancer Institute's Imaging Response Assessment Team network was designed, in part, to address these issues. The Imaging Response Assessment Team sites were to develop mechanisms to integrate their teams into the protocol planning process, as well as to increase clinical collaborations between imaging experts and oncologic investigators [25]. Increased awareness of the role of the radiologist in these trials will be vital to the successful collaboration of imaging experts and oncologists. Many logistic aspects of imaging in clinical trial protocols must be negotiated and resolved. These include, but are not limited to, image acquisition protocol approval, scanner approval, funding allocation for scan acquisition, interpretation and archiving, and performing complete protocol-mandated RECIST measurements. As the science of measuring tumor burden moves forward to include the burgeoning fields of molecular and other biomarker-driven imaging, tumor measurement systems will require translation from clinical trials into clinical practice, and our experience with RECIST will shape our approach to integrating this evolving quantitative technology into clinical practice.

The Radiological Society of North America has formed a coalition, known as the Quantitative Imaging Biomarker Alliance, to facilitate consensus building in the arena of biomarker imaging. The mission of the Quantitative Imaging Biomarker Alliance is to improve the value and practicality of quantitative imaging biomarkers by reducing variability across devices, patients, and time [26]. The National Cancer Institute has also established the Quantitative Imaging Network to support multidisciplinary research teams in developing quantitative imaging methods to measure response to therapy using commercial imaging platforms [9]. Moving forward, it will be vital that all these groups work together and in concert with oncologic subspecialties to establish quantitative imaging standards for oncologic imaging.

Another step toward establishing standards is the Reference Image Database to Evaluate Response to therapy in cancer, a database of CT, MRI, and PET scans of subjects with cancer. The Reference Image Database to Evaluate Response is intended to influence the assessment of software algorithm performance and to help identify imaging-based biomarkers to measure therapy response [27, 28]. A recent publication from the Reference Image Database to Evaluate Response data regarding lung nodules suggests that, to minimize variance across interval examinations, the following advice be adhered to: use the same scanners, maintain the same technical parameters,

use the same patient positioning and breathing, and perform analysis with the same software using the same software settings [29]. These recommendations raise many challenges for tumor measurement. For many large medical centers, it is difficult, if not impossible, to reliably scan a specific patient on a specific scanner. Because patients may be imaged on different scanners, the technical parameters may vary according to detector configuration, table speed, and type of tube current modulation used by each scanner. Furthermore, there is considerable variation in radiologists' performance of linear tumor measurements. A considerable amount of effort from the radiology community will be required to consolidate and standardize tumor metrics to be compliant with research and clinical expectations.

There were limitations to the structure of the survey and, ultimately, the results of our study. The respondents included in this study were limited to large medical centers with cancer centers. The results, therefore, reflect a more academic approach to tumor measurement in patients with cancer, and the opinions and practices of smaller institutions and groups are not reflected here. The respondent population may have skewed results to represent oncologists with strong opinions about the role of imaging in oncology. This bias is inherent in the psychology of response in unsolicited surveys and is too complex to address here.

In conclusion, a large majority of oncologists at National Cancer Institute–sponsored cancer centers think that tumor measurements are necessary for effective routine patient management. Bidimensional measurements of index lesions are preferred in routine oncologic imaging. Less consensus exists as to whether all or a representative subset of tumors should be measured. With respect to cancer therapy clinical trials, there is considerable variability in the implementation of imaging requirements in trial design and the logistical execution of RECIST measurements for clinical trials at these centers.

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FOR YOUR INFORMATION

The reader's attention is directed to part 1 accompanying this article, titled "Quantitative Imaging in Oncology Patients: Part 1, Radiology Practice Patterns at Major U.S. Cancer Centers," which begins on page XXX.

APPENDIX 1: Oncologic Imaging Survey

Respondent Demographics

Select from the following list to describe your subspecialty:
- a. Medical oncologist
- b. Gynecologic oncologist
- c. Radiation oncologist
- d. Other

Select from the following to describe your practice:
- a. Academic teaching hospital
- b. Private hospital with some residencies
- c. Private practice, no residents
- d. Other

How many physicians are in your division?
- a. 0–5
- b. 6–10
- c. 11–15
- d. 16–20
- e. > 20

How many beds are in your hospital?
- a. 0–200
- b. 201–500
- c. 501–750
- d. 751–1,000
- e. > 1,000

Do you see routinely patients in a clinical practice?
- a. Yes
- b. No

What portion of your efforts is clinical patient care?
- a. 0–20%
- b. 21–40%
- c. 41–60%
- d. 61–80%
- e. 81–100%

Select from the following to describe your area of clinical specialty (select all that apply):
- a. Head and neck cancer
- b. Bladder cancer
- c. Renal cancer
- d. Testicular cancer
- e. Breast cancer
- f. Small bowel and/or colon cancer
- g. Pancreatic cancer
- h. Liver cancer
- i. Lung cancer
- j. Prostate cancer
- k. Gynecologic cancer
- l. Melanoma
- m. Sarcoma
- n. Lymphoma
- o. Leukemia
- p. Other (please specify)

New Patient Workup and Imaging

When you see a new patient, do you request that any prior imaging be brought to the first visit (and subsequently added to the radiology PACS archive)?
- a. Always
- b. Sometimes
- c. Never

(Appendix continues on next page)

APPENDIX 1: Oncologic Imaging Survey (continued)

Does your radiology department interpret outside imaging? (Select those that apply)
a. Yes, a report will be rendered and added to our information system
b. Yes, but only as a "hallway consult" (radiologist gives opinion without formal interpretation)
c. No, they will not look at outside imaging
d. I don't know
e. Other (please specify)

What is your expectation of an interpretation of the initial CT scan in an oncology patient?
a. All tumors should be described, measured, and image numbers recorded
b. Some representative tumors should be described, measured, and image numbers recorded
c. The primary tumor should be measured with metastatic lesions described in general terms (i.e., Five liver lesions, the largest of which measures...)
d. Follow RECIST rules for target and nontarget lesions
e. I don't know
f. Other (please specify)

What is your expectation of an interpretation of the follow-up CT scans in an oncology patient?
a. All tumors should be measured and compared with prior scans
b. Measurements can be limited to only the index lesions noted on the original study
c. Measurements can be limited to several index tumor measurements (but not necessarily the same lesions that were previously measured)
d. Tumors can be described as increasing or decreasing, but it is not necessary to give measurements
e. I don't know
f. Other (please specify)

Do you ask radiologists to issue an addendum if tumor measurements are not included in the original interpretation?
a. Always
b. Sometimes
c. Never

Do you think that the radiologist should report tumor measurements routinely in oncology patients who are not enrolled in a clinical trial?
a. Yes, should match the same requirements for trial patients
b. Yes, but I'm not as concerned about the number of lesions measured
c. No
d. I don't know
e. Other (please specify)

What is the appropriate number of lesions measured per organ in a patient who presents with metastatic disease?
a. 1 per organ
b. 2 per organ
c. 5 per organ
d. I don't have a preference
e. I don't know

Imaging in the Oncologic Patient at Your Institution—CT Versus PET

Is it clear to you which malignancies are best evaluated with PET/CT?
a. Yes
b. No

Is there a subset of patients in which you preferentially order PET/CT? (Select all that apply)
a. Head and neck cancer
b. Breast cancer
c. Small bowel and/or colon cancer
d. Pancreatic cancer
e. Liver cancer
f. Lung cancer
g. Urologic cancers (renal, prostate, bladder, testicular)
h. Gynecologic cancer
i. Melanoma
j. Sarcoma
k. Lymphoma
l. Leukemia
m. I don't use PET/CT

(Appendix continues on next page)

APPENDIX 1: Oncologic Imaging Survey (continued)

Are you familiar with NOPR (National Oncologic PET Registry)?
a. Yes
b. No

When you order PET/CT, do you order it with IV contrast?
a. Yes, the majority of the time (depends on malignancy)
b. Yes, the minority of the time (depends on malignancy)
c. No, by my choice (regardless of malignancy)
d. No, my institution does not use contrast for PET/CT
e. I don't know
f. I don't order PET/CT

Do you expect the same type of tumor measurements for PET/CT reports that you get for CT reports?
a. Yes
b. No

Imaging in the Oncologic Patient—Reports

Do you believe it is the radiologist's responsibility to contact you with unexpected findings found on imaging?
a. Agree
b. Disagree
c. I don't know

Select from the following clinical scenarios those that require notification from a radiologist (Select all that apply):
a. Marked progression of disease
b. Acute process requiring immediate medical attention (pulmonary embolus, abscess)
c. Incidental finding requiring long-term imaging follow-up (small pulmonary nodule, incidentally detected hepatic lesion, etc.)
d. Contrast reaction or extravasation
e. Other (please specify)

The Following Are Opinions on Tumor Measurements in Oncologic Imaging

Dictation of all tumor measurements in routine clinical interpretations is the responsibility of the dictating radiologist.
a. Agree
b. Disagree
c. I don't know

Dictation of tumor measurements for several index lesions on routine clinical interpretations is satisfactory to document disease response or progression in routine oncologic imaging.
a. Agree
b. Disagree
c. I don't know

The dictating radiologist may comment on increase or decrease of tumor size without giving tumor measurements to document disease response or progression on routine clinical interpretations.
a. Agree
b. Disagree
c. I don't know

Tumor measurements should be
a. Unidimensional
b. Bidimensional
c. I don't care, as long as one dimension is given (as long as the manner of measurement is consistent)
d. I don't know

When following tumor growth in patients, it is most advantageous to obtain measurements:
a. Based on the index lesions identified in the first study, regardless of interval change
b. Based on the index lesions identified on the most recent comparison
c. Based on the index lesions that show the most significant change in size since the comparison study
d. I don't know

The radiologist impacts patient management when he/she dictates tumor measurements.
a. Agree
b. Disagree
c. I don't know

(Appendix continues on next page)

APPENDIX 1: Oncologic Imaging Survey (continued)

The radiologist impedes patient management when he/she does not dictate tumor measurements.
a. Agree
b. Disagree
c. I don't know

Oncologic Trials

Do you participate in oncologic therapy trials?
a. Yes
b. No

Oncologic Imaging and RECIST

Does your committee, division or department have rules on how RECIST measurements should be handled?
a. Yes
b. No
c. I don't know

Is RECIST measurement an organized process for the oncologic protocols at your institution?
a. Yes, it must be approved by a committee
b. Yes, the oncologists approach the same individual radiologist each time
c. No, it's always an ad hoc issue each time a new protocol is undertaken
d. I don't know
e. Other (please specify)

Is there funding for the person who performs RECIST measurements?
a. Yes
b. No
c. I don't know

If a radiologist is responsible for RECIST measurements, have you included that radiologist in an academic manuscript as a coauthor based on his/her input in performing RECIST measurements?
a. Yes
b. No
c. I don't know

Are you able to distinguish between target and nontarget lesions?
a. Yes
b. No
c. I don't know

In your experience, what is the most common cause of disease progression?
a. Increase in target lesion size
b. Development of new lesions
c. I don't know

Select from the following to reflect your experience with RECIST. RECIST is:
a. Very helpful
b. Flawed, but serviceable.
c. Flawed, and not useful for clinical management of patients.
d. I don't know

Are you familiar with the modifications to RECIST (RECIST version 1.1)?
a. Yes
b. No

Do you think that the reduction in the number of target lesions in RECIST 1.1 (from 10 to 5) reduces accuracy in determining disease response?
a. Yes
b. No
c. I don't know

Process for Approval of Industry-Sponsored Oncology Trials Where End Points Are Dependent on Imaging

Have you been a Principal Investigator in an oncologic therapy trial?
a. Yes
b. No

(Appendix continues on next page)

APPENDIX 1: Oncologic Imaging Survey (continued)

Does your hospital/practice have a centralized committee or process to approve industry-sponsored oncologic trials where imaging is an important component of the protocol end points?

a. Yes
b. No
c. I don't know

Are you required to get imaging protocols approved before initiating an oncologic therapy trial if imaging is included as a therapeutic end point?

a. Yes
b. No
c. I don't know

Do you have a specific person in Radiology to contact with regard to imaging protocol approval before initiating an oncologic therapy trial if imaging is included as a therapeutic end point?

a. Yes
b. No
c. I don't know

Is there a Radiology Committee through which you have to get a budget approval before initiating an oncologic therapy trial if imaging is included as a therapeutic end point?

a. Yes
b. No
c. I don't know

Have you participated in drafting a budget?

a. Yes
b. No

Which of the following have you included in the radiology portion of your budget for an oncologic therapy trial? (Select all that apply)

a. Funding for scan acquisition
b. Funding for image archiving
c. Funding for image interpretation
d. Funding for RECIST measurements
e. None of the above
f. I don't know
g. Other (please specify)