ORIGINAL ARTICLE

Focusing on the “Person” in Personalized Medicine: The Future of Patient-Centered Care in Radiation Oncology

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Abstract

Numerous efforts in radiation oncology aim to improve the value of clinical care. To evaluate the success of these efforts, outcome measures must be well defined and incorporate the beliefs of the patients they affect. These outcomes have historically centered on rates of tumor control, overall survival, and adverse events as perceived and reported by providers. However, the future of patient-centered care in radiation oncology is increasingly focusing on the “person” in the population and the individual in the studies to more closely reflect the ideals of personalized medicine. Formally known as patient-centered outcomes, this metric encompasses parameters of patient satisfaction, engagement, and treatment compliance. Evaluations that investigate the safety and efficacy of treatments are increasingly soliciting participation from patients within a model of shared decision making that improves patients’ knowledge, satisfaction, physical and emotional well-being, and trust in providers. Modern clinical trials that embrace this approach may even focus on patient-reported outcomes as the primary end point, as opposed to time-honored physician-reported events. The authors explore the growing role of patient-centered care, the incorporation of shared decision making, and the relevant body of existing and developing literature on this topic in radiation oncology. The authors report recent discoveries from this area of study and describe how they can not only support high-quality, high-value patient care but also enhance recruitment to clinical oncology trials, both of which are challenging to achieve in today’s relatively resource-strapped environment.

Key Words: Radiation oncology, shared decision making, personalized care, decision aid, quality of life, patient-reported outcomes


INTRODUCTION

What is personalized care in radiation oncology? Although molecular genomics have revolutionized medical oncologists’ ability to distinguish which chemotherapy or targeted agent best suits any individual patient, defining the “personal” patient characteristics that drive decisions to use radiation, and, if so, what type and how much, remain ill defined at present.

Radiation oncology historically has been a field rooted in patient-centered care, with an engrained drive to achieve optimal efficacy against the target, whether for cure or palliation, with minimal morbidity to patients. Although ostensibly this dual-sided but complementary drive has focused on technological innovation, the nontechnical advancements are equally if not perhaps more important to patient satisfaction, engagement, compliance, and ultimately outcomes. Shared decision making (SDM), with or without the use of clinical decision aids (DAs), holds the promise of providing the degree of personalization and patient-centered care for patients in their journey toward discovering the most appropriate radiation treatment plan, including whether radiation is at all appropriate or the modality used. In addition, outcomes research in radiation oncology is increasingly moving to a patient-centered era, with the incorporation of patient-reported adverse events as preeminent end points.
SDM IN ONCOLOGY PERMITS PATIENT-CENTERED CARE

SDM, or the active involvement of patients in considering and ultimately deciding upon their treatment plans jointly with their health care providers, is not a new concept but rather was defined in the late 1990s by Charles et al [1]. Their revised framework, published in 1999, espoused the key hallmarks of SDM as a process that

(1) explicitly identifies different analytic steps in the treatment decision-making process; (2) provides a dynamic view of treatment decision-making by recognizing that the approach adopted at the outset of a medical encounter may change as the interaction evolves; (3) identifies decision-making approaches which lie between the three predominant models (paternalistic, shared and informed); and (4) has practical applications for clinical practice, research and medical education.

Most importantly, the model identifies that patient preferences are taken into account, which previously was not formally recognized in the literature. The concept of SDM has been supported by many national organizations, including NRG Oncology, the American Society of Clinical Oncology, and the Patient-Centered Outcomes Research Institute, which have funded more than 71 comparative clinical effectiveness research studies focused on SDM [2].

Despite this formal definition, there is significant variability in the definition of SDM. The Informed Medical Decisions Foundation defines six steps of SDM, but the steps are broadly defined: invite the patient to participate, present options, provide information on benefits and risks, assist patients in evaluating options on the basis of their goals and concerns, facilitate deliberation and decision making, and implement SDM [3,4]. One group developed an oncology-specific SDM coding system, the Decision Analysis System for Oncology, in early-stage breast cancer, a topic for which there are ample data that patients wish to be actively involved in surgical choice yet are inadequately involved [5]. The investigators found it to be reliable and valid compared with other recognized SDM coding systems such as the OPTION and the Decision Support Analysis Tool [6].

Generally, SDM has been touted for its potential to create more informed patients and family members and to increase trust in the physician-patient relationship. Nonetheless, there have been barriers to physicians using SDM. A German group investigated these challenges using quantitative analysis and found that time and structural constraints and a lack of (multidisciplinary) communication were the most negative aspects of SDM [7].

For the past two decades, groups have investigated the use of SDM to improve patient-centered care [7]. However, few studies have examined SDM in radiation oncology specifically. Shabason et al [8] explored the association between SDM and patient satisfaction during radiotherapy. Interestingly, they found that only about one-third of patients experienced SDM or perceived control in treatment decisions and that these metrics correlated with patient satisfaction. In addition, anxiety, depression, and fatigue were greater in patients who desired but did not perceive control over their treatments.

PATIENT-CENTERED SDM MODELS IN RADIATION ONCOLOGY

SDM models have been conceptually developed, as outlined previously, yet the exact mechanism and features that distinguish them from typical office visits are still being defined. A detailed discussion about the risks and benefits of one treatment over another can constitute SDM, but the most formalized approach is the use of a DA, which can be presented as a printed handbook, a video, or an interactive electronic guide. Clear hallmarks of a DA include a detailed, personalized discussion of treatment options within the context of a patient’s specific demographics, disease-related features, and personal beliefs to help prioritize the patient’s values and goals. The International Patient Decision Aids Standards collaboration has helped define the required elements of a DA. Even in groups of physicians who believe they are using SDM, a minority are using DAs [9]. Like SDM as an overall concept, DAs in oncology also have been proved to promote higher quality decisions [10], patient knowledge, patient-provider communication, patient participation, and decisional satisfaction [11,12]. The largest barrier to routine DA implementation is the system-level support, staffing, and time needed to make DAs part of routine clinical care [11,13]. Embedding DAs into the electronic health record (EHR) has a multitude of potential benefits: (1) it reliably extracts all pertinent clinical information, (2) it prompts providers to offer the use of DAs, (3) it allows sharing of the DA results with the patient through a secure patient portal, and (4) it enables real-time clinical decision support for patients and providers on the basis of the DA results [4]. Despite these benefits, few EHRs are currently able to
accommodate because of the need to merge multiple IT platforms and variable standardization of data elements. As the informatics infrastructure accommodates the use of DAs, it will be critical to embed their use into clinical pathways. Centers that have successfully integrated DAs into the electronic medical record requires desire and interest by key members of any multidisciplinary group, dissemination to all members, and feedback and accountability on system use and performance, based on either “peer pressure” or financial-based incentives [14].

MEASURING THE SUCCESS OF SDM IN RADIATION ONCOLOGY

The appropriate end point of trials investigating SDM is controversial; what is the best surrogate end point or metric for patient-centered care? Brundage et al [15] outlined short- versus long-term outcomes, including shorter term provider and patient outcomes (satisfaction with decision-making process and patient-provider partnership, confidence in decision, patient trust in provider, self-efficacy, mental health, physical and emotional well-being) and longer term patient outcomes (treatment adherence, quality of life (QOL), and remission). Internationally, Germany adopted SDM as part of new melanoma guidelines and used a longitudinal questionnaire to determine the value, finding that more than 80% of patients, according to the Control Preference Scale, wanted to play an active role and found a preference shift in 43% of patients toward active involvement [16]. Perhaps the strongest end point of the use of SDM has been shown in palliative care, in which SDM decreased the odds of receiving chemotherapy in the last 14 days of life and of dying in an acute care setting, two well-validated markers of higher quality palliative care [12]. In radiation oncology, it is unclear what the best metric of success using SDM will be. Patient satisfaction, trust in providers, and physical emotional well-being are consistently useful metrics; it is not yet established the best way to integrate these metrics into alternative payment models, but there are a variety of pilot programs using these tools as part of reimbursement strategies [17].

CURRENT RADIATION ONCOLOGY TRIALS IN SDM AND DAs

In the contemporary radiation oncology environment, any additional steps to routine clinical care must be clearly justified by validated research. Research programs evaluating SDM and the value of DAs have been increasing steadily, with four recently completed or currently open trials (as of July 5, 2016) evaluating the utility of DAs as their primary method (Table 1). The primary end points of these studies include decisional conflict scale scores, self-efficacy, uncertainty, and knowledge and preference scores.

QOL AND PATIENT-REPORTED OUTCOMES IN RADIATION ONCOLOGY CLINICAL TRIALS

A focus on QOL has been a central premise of radiation oncology practice for many years and represents a way in which patient-centered care has been integral to radiation oncology practice. RTOG® and its successor organization, NRG Oncology, have been frontrunners in this regard. For example, prior RTOG studies have demonstrated that QOL significantly predicts outcomes, including local control and survival [18-20]. QOL has also helped better define the potential role and benefit of more sophisticated technologies in radiation oncology, such as intensity-modulated radiation therapy (RT) [21]. Furthermore, the importance of considering family support networks to cancer survival was demonstrated by Konski et al [22], who noted that men without partners had inferior survival on multivariate analysis compared with married men or other men with partners. Metrics and methods developed by RTOG have helped establish the centrality of patient- and family-centered care in the practice of radiation oncology.

Increased recognition of the importance of patient-reported outcomes (PROs) is another way that patient-centered care has been translated into radiation oncology. PROs have been recognized for more than a decade, but unlike more traditional oncologic end points, widespread adoption of PROs has been hampered by inconsistency in terminology and use. Patient toxicity has typically been reported by the provider-generated National Cancer Institute (NCI) Common Toxicity Criteria for Adverse Events (CTCAE). However, multiple studies have shown the discordance between provider and patient toxicity reporting [23,24], and therefore there has been a priority to make PROs a critical end point in many studies, particularly comparative effectiveness research. More recently, this important metric has begun to take a preeminent position as a validated end point in many trials [25]. There are multiple validated PRO instruments, including the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire...
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Note: BCS = breast-conserving surgery; DA = decision aid; DCIS = ductal carcinoma in situ; RT = radiation therapy; SBRT = stereotactic body radiation therapy.
Core QLQ-C30, the Functional Assessment of Cancer Therapy, the MD Anderson Symptom Inventory, the Patient-Reported Outcomes Measurement Information System, and, most recently, PRO-CTCAE [23]. PRO-CTCAE was developed starting in 2008 to decrease heterogeneity in patient-centered data after careful analysis by the NCI, with the purpose of complementing existing safety and tolerability assessments across cancer clinical trials [26,27]. This measurement has been analyzed as a valid, reliable, and responsive instrument, and results are favorable in a diverse population and in comparison with other QOL scale changes [28,29]. Limitations of the PRO-CTCAE include lack of validation in surgical and non-English-speaking patients.

Ultimately, a key goal is for PROs to be a primary end point in appropriate clinical trials to define the next standard of care based directly on patients’ perspective. For example, in treatment comparisons that are hypothesized to have no significant difference in traditional objective clinical outcomes, such as progression-free survival, PROs can be a useful primary end point in trials if it is hypothesized that the two treatments have different adverse events or other clinically relevant outcomes, such as fewer missed work days or preservation of ability to work. Indeed, in radiation oncology, more studies are being designed precisely this way [24]. RTOG has ongoing trials in which PRO end points are not only integral elements of the studies but are in fact the primary objectives. For example, RTOG 0938 (A Randomized Phase II Trial of Hypofractionated Radiotherapy for Favorable Risk Prostate Cancer) is a randomized phase 2 trial comparing two hypofractionated radiation regimens. The bladder and bowel domains of the Expanded Prostate Cancer Index Composite instrument are being used to measure health-related QOL as the primary end point of that study. The trial has been completed, design of the successor trial is under way, and QOL outcomes will be an important part of the new trial [30]. The Prostate Advanced Radiation Technologies Investigating Quality of Life trial is an exciting example of a randomized study to incorporate a sole PRO (Expanded Prostate Cancer Index Composite bowel score) as the primary end point [31]. In addition, QOL holds the promise of enhancing clinical care as a method of communication from patients to providers to communicate symptoms that need to be addressed in real time [32]. More and more, efforts are under way to incorporate QOL into the radiation oncology clinic workflow directly.

AN EXAMPLE OF PERSONALIZED CARE FROM SDM TO PATIENT-CENTERED RESEARCH: EARLY-STAGE NON-SMALL-CELL LUNG CARCINOMA

Lung cancer is the leading cause of cancer-related mortality. For patients with stage I non-small-cell lung carcinoma (NSCLC), the standard of care remains surgery for those who are operable, and over the past decade, stereotactic body RT (SBRT) has emerged as the highly effective standard therapy for patients who cannot tolerate or decline surgery [33].

Given its safety profile, and unexpected primary tumor control rates that exceed 90%, three phase 3 randomized studies were opened between 2008 and 2010 to evaluate SBRT as an alternative to surgery in operable patients. However, recruitment to these trials was challenging, as patients were commonly approached during surgical consultations, which did not provide the optimal equipoise between radiation and surgery if they were labeled “medically operable.” Although each of these trials was closed in 2013 because of poor accrual, a new generation of randomized studies currently seeks to recruit patients to similar trials using modified strategies. These include the STABLE-MATES (JoLT-Ca Sublobar Resection [SR] Versus Stereotactic Ablative Radiotherapy [SAbR] for Lung Cancer; ClinicalTrials.gov identifier NCT02468024), SABRTooTH (A Study to Determine the Feasibility and Acceptability of Conducting a Phase III Randomised Controlled Trial Comparing Stereotactic Ablative Radiotherapy With Surgery in Patients With Peripheral Stage I Non-Small Cell Lung Cancer Considered Higher Risk of Complications From Surgical Resection; ClinicalTrials.gov identifier NCT02629458), and VALOR (Veterans Affairs Lung Cancer Surgery or Stereotactic Radiotherapy; Veterans Affairs Cooperative Study Program 2005) studies. The recruitment schema for STABLE-MATES (n = 258) randomizes patients before seeking consent in a process known as the Zelen design, SABRTooTH (n = 58) protects patients from bias by limiting contact with surgeons and/or radiation oncologists until pulmonologists can complete the consent and randomization process, and VALOR (n = 670) aims to safeguard patients from bias by educating patients about two potentially equivalent treatment options before a navigated consent process in which research associates accompany patients during surgical and radiation oncology consultations [34]. The success of each of these trials will provide meaningful insights into the value of SDM during recruitment to difficult randomized trials.
However, the results of these trials may not be available for many years to come.

The conundrum posed by a lack of completed randomized trials for this disease is highlighted by the results of a pooled analysis of the prematurely closed ROSEL (Trial of Either Surgery or Stereotactic Radiotherapy for Early Stage [IA] Lung Cancer; ClinicalTrials.gov identifier NCT00687986) and STARS (Randomized Study to Compare CyberKnife to Surgical Resection in Stage I Non-Small Cell Lung Cancer; ClinicalTrials.gov identifier NCT00840749) trials that demonstrated a statistically significant 16% overall survival advantage with SBRT at 3 years [35]. Although such a comparison was underpowered (n = 58 of 1,990 planned), the findings are a likely contributor to an ongoing shift from surgery to SBRT for early-stage NSCLC.

Clinicians may look to the literature to guide decisions, including studies that demonstrate no declines in QOL after lung SBRT [36]. However, clinician perceptions of the available data are variable, as recently shown in a binary-choice experiment between SBRT and surgery that revealed strong specialty biases, further underscoring the importance of SDM [30].

Given the dilemma outlined here, a patient-centered approach may be critical when counseling patients with operable stage I NSCLC. This might be particularly important if a goal is to minimize decisional regret, and multiple organizations including the Patient-Centered Outcomes Research Institute, have prioritized funding SDM in both the screening and treatment of lung cancer. At the University of Pennsylvania, efforts are underway to develop and validate a personalized, web-based, electronic DA for patients with early-stage NSCLC choosing between SBRT and surgery, and these data will be used in a randomized trial with the primary end point of decisional conflict [37,38]. The secondary end points incorporate additional patient-centered outcomes, including QOL (VR-36), emotional distress (Impact of Event Scale), and patient-centered communication. Studies such as this will hopefully provide much needed guidance for patients and clinicians whenever there is an absence of high-level evidence for any disease when more than one treatment option is available.

CONCLUSIONS AND FUTURE DIRECTIONS
The future will undoubtedly be defined by the various stakeholders in patient-centered research in radiation oncology. The critical and most evident beneficiary of patient-centered research is the patient, whether incorporating a DA into the patient-physician conversation or incorporating PROs into critical, practice-changing trials. Patient advocacy groups, including the NCI’s Advocate in Research Working Group, are constantly supporting patient-centered research both in the clinic and in investigations in radiation oncology [39]. Physicians and health systems are eager to incorporate DAs into routine clinical care, the EHR, and consensus clinical pathways, which have been shown to improve consistent quality [14]. Educators are recognizing that they must specifically train physicians in how to approach an SDM model [40]. Moreover, physician groups are equally engaged in pushing forward a patient-centered research agenda; NRG Oncology has a focused patient-centered outcomes research committee that aims specifically to focus on these issues and the American Society of Clinical Oncology’s Value Framework Project was recently revised to specifically call for a patient-centered oncology model [41]. Last, insurers, beyond starting to think about how to compensate appropriately for high-quality, patient-centered care, are considering how to specifically reimburse for the resources required to build DAs and participate in validated SDM.

Personalized RT will be greatly enhanced with SDM and PROs in the clinical and research setting; at the same time, the field is also fortunately rife with other essential aspects of “personalized” RT: molecular genomics that may allow RT dose escalation or de-escalation, including current successful ongoing de-escalation efforts in human papillomavirus–positive head and neck cancer; real-time adaptive radiation replanning, such as real-time imaging with MRI or the ongoing RTOG 1106/ACRIN® 6697 Randomized Phase II Trial of Individualized Adaptive Radiotherapy Using During-Treatment FDG-PET/CT and Modern Technology in Locally Advanced NSCLC, investigating changing RT fields on the basis of functional PET images midway through treatment to allow safer and more effective RT dose escalation. Moreover, research is under way unifying QOL outcomes with the underlying genetics at a molecular level in the establishment of the GeneQol Consortium, which is the ultimate way of integrating “personalized” medicine at various levels [42]. Taken together, the future of radiation oncology will be highly specialized and based on integrating the whole person and his or her molecular fingerprint.

We are confident that our field, particularly through the strong efforts of NRG Oncology, is focusing on personalized medicine at multiple levels and helping
define the future of patient-centered care in radiation oncology through SDM using DAs, validated metrics, and driving PROs in the front seat, where they belong.

**TAKE-HOME POINTS**
- SDM has been identified as a key element of high-quality, patient-centered care and has been associated with improved patient knowledge and satisfaction, physical and emotional well-being, and trust in providers.
- In radiation oncology, growing attention has been devoted to developing and systematically investigating patient DAs to aid patients in their treatment choices.
- QOL metrics significantly predict outcomes, including local control and survival, and PROs are increasingly being used in routine patient-physician communication and incorporated as primary end points in critical prospective trials.
- SBRT for early-stage NSCLC has emerged as an excellent alternative to surgery in selected situations, and the ongoing trials represent useful examples of organized SDM and incorporation of PROs.
- NRG Oncology and its legacy cooperative groups have been long-standing supporters of patient-centered outcomes and continue to drive forward oncology trials using validated QOL data and PROs.

**ADDITIONAL RESOURCES**
Additional resources can be found online at: http://dx.doi.org/10.1016/j.jacr.2016.09.012.

**REFERENCES**


