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uncertainties of adjuvant therapies for incompletely resected early-stage NSCLC, it is appropriate to emphasize here again that repeated resection, when possible, is the preferred treatment for incompletely resected early-stage NSCLC.

Kareem Ibrahim, MD

Bryan M. Burt, MD

Division of General Thoracic Surgery

Department of Surgery

Baylor College of Medicine

Houston, Tex

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THE VALUE OF COLLABORATION BETWEEN THORACIC SURGEONS AND RADIATION ONCOLOGISTS WHILE AWAITING EVIDENCE IN

OPERABLE STAGE I NON-SMALL CELL LUNG CANCER

To the Editor:

In the closing remarks of an editorial recently published in the *Journal*, Schaheen and D'Cunha¹ highlight the challenge for thoracic surgeons to adequately compare the efficacy of surgical resection and stereotactic body radiation therapy (SBRT) for patients with operable stage I non-small cell lung cancer (NSCLC).¹ We agree with their comments that “our patients aren’t fully able to dissect the literature and the nuances of the trials”¹ that have been published in the peer-reviewed literature and then recycled in the lay media with sensationalized headlines.² It is for this reason that a multidisciplinary committee of experts across

radiation oncology and thoracic surgery recently published the ASTRO (American Society for Radiation Oncology) SBRT evidence-based guideline for early-stage NSCLC and addressed this topic as a key question: “When is SBRT appropriate for patients with T1-2, N0 NSCLC who are medically operable?”³

On the basis of a systematic review of the literature for patients in medically operable condition, our recommendation is that for “patients with ‘standard operative risk’ (ie, anticipated operative mortality of <1.5%), lobectomy with systematic mediastinal lymph node evaluation remains the recommended treatment,” whereas “discussions about SBRT as a potential alternative to surgery are encouraged” for patients with higher operative risk.³ At the same time, we also recommend that “any patient with operable stage I NSCLC being considered for SBRT should be evaluated by a thoracic surgeon, preferably in a multidisciplinary setting to reduce specialty bias.”³

Although we also agree with Schaheen and D'Cunha¹ that a nonoperative therapy for patients with early stage lung cancer who are fit enough for surgery needs to be carefully evaluated and adequately compared with the long-established standard of care of surgical resection, we have reached a point in time when surgery is not the only treatment choice,⁴ and the available data simply do not shed adequate light to help us know which treatment is optimal for any given patient. To some, such a statement may be considered heretical. Yet, recent attempts at randomized comparisons between surgery and SBRT provided only preliminary and underpowered findings,⁵ and did not provide a signal that surgery was superior.⁶ In fact, the only time that surgery was shown to be superior in a randomized trial was in 1963, when it was compared to palliative doses of radiotherapy.⁷ It is insightful to note that this was more than a decade before the introduction of computed tomography that allows 3-dimensional targeting and more than 30 years before the first patient with lung cancer was treated with SBRT.⁶

Notwithstanding, investigators continue publishing retrospective studies that compare these two treatments, such as the referenced analysis by Yerokun and colleagues.⁸ Unfortunately, evaluations of large observational data sets are inherently imperfect as a result of unavoidable confounding factors that cannot be overcome with propensity matching because of a long-standing reservation of SBRT for patients with poorer performance statuses and shorter life expectancies. Data sets such as the NCDB (National Cancer Database) and SEER (Surveillance, Epidemiology, and End Results Program) provide important insights into cancer care and ideal opportunities to use biostatistics and propensity matching to understand outcomes better. Yet, the absence of specific information on the severity of comorbidities and pulmonary function makes their applicability to this subject limited given that those are

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among the strongest variables that predict short- and long-term survival and, more importantly, are hallmarks used for selecting patients for surgery or SBRT.

We share the concern of Schaheen and D'Cunha¹ regarding risk of occult nodal disease in clinical stage I NSCLC, but we are intrigued by their reference to CALGB 9761, a trial performed largely in the pre-positron emission tomography era.⁹ In addition, the 38.3% of patients in that study with an inaccurate preoperative clinical stage and diagnosis did not have this occur solely because of nodal upstaging, as suggested by Schaheen and D'Cunha,¹ especially considering that more than 13% of all patients had either benign disease or a malignancy other than NSCLC. Unfortunately, the data from that trial are no longer relevant in the current era, in which occult lymph node metastasis rates are commonly lower than 15% with the integration into staging of positron emission tomography with computed tomographic imaging.^{10,11} Although it remains a long-standing belief that earlier identification of N1 or N2 disease can improve outcomes with earlier initiation of secondary therapies, it is important to consider that the benefit of this approach may not outweigh the mortality risks associated with “surgery for all.” As Louie and colleagues¹² have modeled, for every 100 patients who undergo surgical staging of the mediastinum, approximately 15 may have upstaging with N1 or N2 disease, and of these, 10 are typically fit enough for postoperative chemotherapy that leads to a 5% improvement in survival at 5 years. This leads to a calculated 0.5 patients of the original 100 patients—1 of 200—benefiting from surgical staging, a benefit that disappears if the surgical mortality exceeds 0.5%.

Meanwhile, data for the use of up-front SBRT for patients fit enough for surgery continue to grow. While most reports on SBRT have limited follow-up compared to surgical series, they have demonstrated local control and cancer-specific survival that are often as good as or even better than surgical reports in the literature. Series in the literature report 3- and 5-year overall survivals with SBRT ranging between 77% and 95%^{6,13-16} and 51% and 74%,¹⁴⁻¹⁸ respectively, with 5-year cause-specific survivals of 82% to 90%.¹⁶ While these outcomes may lend enthusiasm for some to recommend SBRT as an alternative to “avoid the knife,” we stand with Schaheen and D'Cunha¹ in advising that until definitive data exist, treatment decisions for patients who are fit enough to undergo operation are best made by a multidisciplinary team that includes experienced thoracic surgeons, radiation

oncologists, and medical oncologists who work together and are focused on the best interest of each and every patient.

By many accounts, practice patterns have already begun to shift, and surgical patients are increasingly opting for SBRT.¹⁹ Because the full consequences of such decisions remain unclear, it is the duty of radiation oncologists and thoracic surgeons to support the enrollment of patients in the currently active trials that are randomly allocating patients between resection and SBRT, including VALOR (Veterans Affairs Lung Cancer Or Stereotactic Radiotherapy; NCT02984761), STABLE-MATES (JoLT-Ca Sublobar Resection (SR) versus Stereotactic Ablative Radiotherapy (SAbR) for Lung Cancer; NCT02468024), and POSTILV (Radical Resection vs Ablative Stereotactic Radiotherapy in Patients With Operable Stage I NSCLC; NCT01753414). Data from these trials are needed more than ever to inform and guide our multidisciplinary decisions for patients with early stage NSCLC who are fit enough to undergo lung cancer surgery, but may instead be more interested in SBRT.

Drew Moghanaki, MD, MPH^a

Charles B. Simone II, MD^b

Andreas Rimner, MD^c

Tomer Z. Karas, MD, FACS^d

Jessica Donington, MD^e

Shervin M. Shirvani, MD, MPH^f

Megan Daly, MD^g

Gregory M. Videtic, MD, CM, FRCPC, FACP^h

Benjamin Movsas, MD, FASTROⁱ

On behalf of the ASTRO Evidence-Based Guideline Committee for Stereotactic Body Radiation Therapy (SBRT) for Early-Stage Non-Small Cell Lung Cancer

^aRadiation Oncology Service

Hunter Holmes McGuire VA Medical Center and Virginia

Commonwealth University

Richmond, Va

^bDepartment of Radiation Oncology

University of Maryland

Baltimore, Md

^cDepartment of Radiation Oncology

Memorial Sloan Kettering Cancer Center

New York, NY

^dDepartment of Cardiothoracic Surgery

Miami VA Healthcare System

Miami, Fla

^eDepartment of Cardiothoracic Surgery

New York University

New York, NY

^fDepartment of Radiation Oncology

Banner MD Anderson Cancer Center

Phoenix, Ariz

^gDepartment of Radiation Oncology
University of California
Davis, Sacramento, Calif

^hDepartment of Radiation Oncology
Cleveland Clinic
Cleveland, Ohio

and ⁱDepartment of Radiation Oncology
Henry Ford Cancer Institute
Detroit, Mich

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THE BURDEN OF PROOF

Reply to the Editor:

The erudite letter from the ASTRO Evidence-Based Guideline Committee for Stereotactic Body Radiation Therapy (SBRT) for Early-Stage Non-Small Cell Lung Cancer (ASTRO Group)¹ carries a title that all clinicians managing lung cancer could easily agree on. Conversely, the style of the letter is typical of a diplomatic effort that may not to stand the test of time because of the underlying biases of both radiation oncologists and thoracic surgeons.

Surgeons should be glad to learn that the ASTRO Group¹ agrees that the currently available evidence does not permit patients to draw crucial information regarding their own health management pathway independently from the intricacies of the literature. Better late than never—at this time, a balanced perspective toward which procedure is indicated is needed as clinicians clearly weigh the evidence in the literature differently depending on their specialty.²

In addition, thoracic surgeons keep on retrospectively analyzing large databases with propensity score matching to compare wedge and lobectomy with SBRT.¹ Although this statistical methodology is imperfect, radiation oncologists have also used the same methodology to the benefit of SBRT.³

Moreover, thoracic surgeons are appropriately not convinced by reading the SBRT literature, which is filled with failed randomized trials and related mathematical acrobacies.⁴ At the same time, there are diverse interpretations of SBRT—SBRT for peripheral,⁵ SBRT for central,⁶ and SBRT for ultracentral lung tumors.⁷ In fact, there is one SBRT approach for lung tumors larger than 5 cm (cT3) as opposed to smaller lesions⁸—a major leap “forward” compared with the “no-fly zone” concept.⁹ Of course, thoracic surgeons adapt the extent of resection as radiation oncologists modulate SBRT dosage in an attempt to strike a balance between the needs for oncologic completeness and reduced mortality and morbidity.⁹ If radiotherapists do what surgeons do, it means that they want to avoid similar problems¹⁰⁻¹³ that are underreported in the SBRT literature, with potentially harmful consequences to patients.^{14,15}