Management of Stage I Lung Cancer with Stereotactic Ablative Radiation Therapy

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KEYWORDS

• SBRT • SABR • SRS • Stereotactic • Ablative • Hypofractionation • Lung cancer

KEY POINTS

- The incidence of early stage lung cancer is increasing owing to the adoption of lung cancer screening guidelines.
- Although surgery has been considered the historical standard for early stage disease, there is no level I evidence supporting its use over modern radiation therapy.
- Stereotactic ablative radiation therapy (SABR) is an emerging treatment option for patients with early stage disease that is distinctly different that conventional radiation therapy in both conduct and radiobiologic effect.
- Although unable to successfully accrue in the past, current studies are attempting to directly compare SABR versus surgery in operable patients.

INTRODUCTION

Early stage non–small cell lung cancer (NSCLC) is a growing clinical entity with evolving standards of care. As a whole, NSCLC is the second most common malignancy in men and women, with 224,390 new cases and 158,080 deaths predicted in 2016.[1] It remains the leading cause of death from cancer, with a 5-year overall survival of approximately 21%.[2] Deaths attributable from lung cancer are driven primarily from advanced disease, with early stage disease considered potentially curable. Although most patients have traditionally presented with late stage disease, the population of patients with early stage lung cancer is now expected to increase significantly due to improvements in diagnostic modalities and the widespread adoption of lung cancer screening programs.[3]

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In 2014, lung cancer screening with low-dose chest computed tomography (CT) was recommended for high-risk individuals by the US Preventive Services Task Force based on several large, population-based studies.[4] The largest US-based trial was the National Lung Screening Trial, a national study accruing more than 50,000 patients demonstrating reduced lung cancer mortality with low-dose CT screening. In this study of high-risk individuals with 30 or more pack-year smoking history between the ages of 55 to 74 years of age, the relative risk of mortality from lung cancer decreased by one-fifth. Based on these results, several societies and national organizations have endorsed guidelines for lung cancer screening.[5–7] The adoption of lung cancer screening guidelines is expected to significantly increase the detection of early stage disease. As the incidence of early stage lung cancer increases, it will be critical to better define appropriate treatment options for patients in this population.

TREATMENT OPTIONS FOR EARLY STAGE NON–SMALL CELL LUNG CANCER

For decades, the historical standard for early stage NSCLC was surgical extirpation. Similar to early treatment paradigms for breast cancer, the best chance of cure was thought to be achieved through radical surgery. As a result, the standard of care endorsed by nearly all oncologic and surgical societies was centered around surgery as the cornerstone of treatment.[8] To date, surgery remains the favored approach, as current National Comprehensive Cancer Network guidelines recommend complete surgical resection as the preferred therapy for localized disease in patients who can tolerate the procedure.[9]

However, the role of surgery as the de facto definitive approach has increasingly come under inquiry as the evidence has not yet been established through randomized trials. Three randomized phase 3 trials have been attempted to directly compare surgery versus radiation, but all have prematurely closed due to poor accrual.[10,11] Consequently, there continues to be considerable debate as to what constitutes standard treatment options. The evidence for the use of surgery primarily relies on principles of oncologic management and early outcome data from selected groups of patients in surgical series.[12] Furthermore, for many years, the only viable treatment option to address gross disease was limited to surgery. Historical delivery of radiation often yielded poor outcomes using conventional fractionated radiotherapy. The use of large treatment fields due to targeting uncertainty limited the ability to deliver truly therapeutic doses, resulting in toxic treatment with poor local control rates.[13] Similar to data demonstrating potential harm in postoperative lung patients, the delivery of antiquated thoracic radiation has traditionally resulted in an unfavorable therapeutic ratio.[14] Consequently, radiation was primarily reserved in the cases of palliation. However, as technological advances rapidly came into adoption and radiation treatment techniques became more sophisticated, effective local control of disease became increasingly achievable. As the population of early stage NSCLC continues to grow, elucidating the role of radiation therapy in the definite management of early stage disease will become a more salient issue.

DEVELOPMENT OF STEREOTACTIC ABLATIVE RADIATION THERAPY

The development of key techniques in stereotactic delivery has transformed the treatment of early stage lung cancer over the past 2 decades. Beginning in the late 1980s, several investigators across the globe began experimenting with the use of larger and more targeted doses of radiation to extracranial targets based on techniques implemented from intracranial radiosurgery. Initially deriving its nomenclature from these intracranial techniques, the original term stereotactic body radiation therapy (SBRT)