The case for SABR as the global standard for non-operable early-stage non-small cell lung cancer

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External beam radiotherapy, delivered in divided 'fractions' over many weeks, has historically been the standard treatment for early-stage non-small cell lung cancer (ES-NSCLC), in patients unfit or unwilling to have surgery. Over the past two decades, stereotactic ablative radiotherapy (SABR — also called stereotactic body radiotherapy or SBRT), a highly conformal, high dose-per-treatment, abbreviated form of radiotherapy, has supplanted conventionally fractionated radiotherapy (CFRT) in many regions globally. Made possible by advances in imaging, patient immobilization, and radiation-delivery technology, SABR's increasing utilization across many indications has been driven by improved efficacy, patient-convenience and reduced resource utilization. In ES-NSCLC, there has been widespread adoption of SBRT for patients ineligible for surgery, supported by substantial evidence demonstrating excellent local control with an acceptable toxicity profile, comparing favourably to similar series of CFRT.[1] More recent randomized evidence include the Phase-III CHISEL trial, which demonstrated superior overall survival (OS) and local control,[2] whereas the Phase-II SPACE trial failed to demonstrate significant oncologic benefit (i.e. OS).[3] In this scenario where new technology is being adopted with potential clinical benefits, the question of cost-effectiveness is of particular importance for patients, healthcare providers and payers.

In their publication, "Cost-effectiveness of stereotactic body radiotherapy versus conventional radiotherapy for the treatment of surgically ineligible stage I non-small cell lung cancer in the Brazilian public health system", Arruda et al.[4] highlighted that SABR is not yet funded by the public healthcare system in Brazil for ES-NSCLC, even though it is recommended by guidelines elsewhere in the world.[5] The authors developed a Markov model to assess the cost-effectiveness of SABR compared to CFRT in the treatment of ES-NSCLC, in the context of Brazilian public health care system. This study was robust methodologically, including the use of outcomes derived from randomized trials, a lifetime time-horizon, detailed sensitivity analyses, and compliance with the Consolidated Health Economic Evaluation Reporting Standards.[6] While similar analyses have been performed around the world, it is critical to consider regional payer-models, population factors, costs and willingness-to-pay thresholds to generate a representative and region-specific cost-effectiveness analyses. SABR was cost-effective compared to CFRT in 92% of probabilistic sensitivity scenarios, and at an incremental cost-effectiveness ratio (ICER) of only $65.16 USD per quality-adjusted life year (QALY) gained. Willingness-to-pay thresholds vary around the world, and while Brazil does not currently have an accepted threshold, the World Health Organization proposal of three times gross-domestic-product per capita (in Brazil ~$20,000 USD) strongly supports funding this valuable therapy.

This publication provides a valuable contribution to the body of investigations on the health economics in ES-NSCLC. Sher et al compared SBRT to CFRT and radiofrequency ablation, finding SABR to have an ICER of $6,000 USD per QALY over CFRT, from the perspective of an American third-party payer.[7] This finding was reliable over several sensitivity analyses. Louie et al utilized cancer-risk management model to compare the cost-effectiveness of SABR and other treatment modalities (surgery, CFRT, supportive care) in a Canadian public-payer context, showing SABR to dominate CFRT.[8] The analysis also highlighted the magnitude of absolute clinical and financial benefit when applied to the entirety of a publicly funded health care system. Grutters et al compared SABR to CFTR and heavy-particle therapy, and found SABR to dominate CFTR in a European public healthcare context.[9] While these and other analyses have consistently shown cost-effectiveness advantages with SABR, diagnostic and treatment pathways, cost-structures, and willingness-to-pay thresholds can vary dramatically around

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the world, raising the importance of region-specific analysis. Further, prior studies rarely reported QALY endpoints, and utilized outcome probabilities from older, lower quality evidence available, highlighting the value of this newer Brazilian model.

SABR has been shown cost-effective in other cancer contexts as well. Within ES-NSCLC, analysis comparing SABR to surgery in 'marginally' operable patients showed SABR to be dominant, though lobectomy remained dominant in operable patients.[10] Moreover, SABR (or other hypofractionated regimens) has proven cost-effective over CFRT in prostate, brain metastases, and other malignancies.[11] Indications for SABR continue to be explored, necessitating further cost-effectiveness assessments.

While the evidence to support SABR in ES-NSCLC adoption grows, there remain outstanding questions. Ongoing investigations include optimal dosing and fractionation of SABR, the role of immunotherapy with or following SABR, the value of heavy particle (proton and carbon ion) irradiation, safety of treatment in tumours with ultra-central location, and the potential role for SABR in operable patients.

With the potential to decrease the utilization of highly limited linear accelerators in Brazil, SABR adoption in ES-NSCLC may improve access to life-saving treatments for other patients. The authors wisely highlight that while this will require upfront investment to add public-system capacity, the clear ICER advantage, well below global willingness-to-pay thresholds, justifies the upfront costs. For patients, SABR likely reduces out-of-pocket costs by limiting hospital trips. Context-specific cost-effectiveness analyses continue to play a valuable role in supporting the funding and adoption of emerging therapies. SABR, with fewer treatments and increased efficacy in many settings when compared to CFRT, is likely to see increasing adoption globally, across many cancer types. This analysis serves an important step toward increasing access to a valuable treatment in Brazil and should be used as a template to evaluate the adoption of SABR in other systems.

Contributors

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Declaration of interests

A.M. nothing to declare.

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