Ablative therapies for lung metastases: a need to acknowledge the efficacy and toxicity of stereotactic ablative body radiotherapy

We read with interest the single institutional results of radiofrequency ablation (RFA) for pulmonary metastases reported by Thierry de Baère et al. [1]. We congratulate the authors in publishing the largest series to date in this setting. They performed RFA in relatively small tumours with a median size of 15 mm, with 70% of tumours being 2 cm or less in size, and reported local failure rates of 5.9% and 8.5% at 1 and 2 years, respectively, while other authors have reported similar short-term local control rates after RFA, analysis of post-RFA surgical resections have found evidence for complete tumour cell necrosis in only 37.5% of cases, with scattered vital tumour tissue present in 50% of tumours measuring 3.5 cm or less [2]. A recent review highlighted relatively small evidence base for RFA exists in this setting, concluding that local control must be ‘measured against that achieved by stereotactic radiotherapy’ [3]. Surprisingly, de Baère et al. make no reference at all in their article to the role of stereotactic ablative radiotherapy (SABR) for patients with pulmonary metastatic disease.

SABR is a non-invasive technique that affords comparable control rates for lung metastases, with our own group recently reporting 93% local control rates at 2 years in a smaller cohort of 65 patients [4]. Rates of local control similar to these have been reported in recent randomized, controlled trials of SABR versus surgery for operable primary lung cancer [5], where the 3-year freedom from local recurrence was 96% in the SABR group, compared with 100% for patients in the surgery group (log-rank P = 0.44). Importantly, toxicity rates are low after SABR for pulmonary metastases, with published series showing consistently less than a 5% incidence rate of grade 3+ toxicities (or those requiring hospitalization) [6]. In contrast, de Baere et al. indicate that 25% of their patients receiving RFA required hospitalization exceeding 4 days, and report two patient deaths in the early post-treatment period. They also reported pneumothoraces after 67% of the procedures, which resulted in a chest drain insertion tube in 58%. In light of the significant disparity between the toxicity rates observed in this study in comparison to those reported for SABR, readers should be aware of all ablative options currently available for patients with multiple pulmonary metastases.

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Reply to the letter to the editor ‘Ablative therapies for lung metastases: a need to acknowledge the efficacy and toxicity of stereotactic ablative body radiotherapy’ by Siva et al.

We are delighted with the interest shown by Dr Siva in reading our paper and we thank him for his comments [1]. Contrary to the first word of Dr Siva’s letter, the reported study [2] is not ‘single institutional results’ but a bicentric result...
from Gustave Roussy (Villejuif) and Bergonié Cancer Center (Bordeaux).

As acknowledged by Dr Siva in his letter, others have reported similar control rate, and the study by Schneider et al. referenced by Dr Siva with a 37.5% complete necrosis with radiofrequency ablation (RFA) is among the worst results ever published with RFA. In fact, these reports deal with a very unusual RFA technology (bipolar or multipolar RFA), delivered without image guidance (ablation guidance was obtained with per-operative palpation during thoracotomy). This series emphasizes that lung RFA is not an effective per-operative technique, and needs image guidance. Indeed, as explained in our publication, CT guidance is the key for treatment success in lung metastases. The air density of the lung parenchyma together with tissue density of the target tumor and metallic density of the RF needle, allows for optimal contrast at imaging, and with the help of 3D and multiplanar reconstruction, it allows for very high accuracy in treatment targeting and delivery, thus probably explaining the high success rate we reported. It is noticeable that, using such a technique, 100% of necrosis has been found at pathology in 9 of 9 lung metastases measuring 1–3 cm treated with RFA within 4 weeks before surgical resection [3].

Another factor that can explain our high success rate is the use of general anesthesia, because it has been reported that peri-procedural pain occurred in 29% of cases with 3% of treatment interrupted due to pain when using conscious sedation [4].

The rate of chest tube placement reported in our publication is not 58% of the overall population as written by Dr Siva, but chest tube placement occurred in 58% of the 67% patient demonstrating a pneumothorax, which is 38% of the overall population. We consider chest tube placement as an expected side-effect and not as a complication; moreover, that the vast majority of chest tubes are retrieved before Day 2. We have to remember that surgery drained every single patient with large bore chest tube. Concerning stereotactic ablative radiotherapy (SABR), it has been reported that placement of fiducial markers needed for SABR has resulted in 33.3% pneumothoraces (Major: 13.3%; Minor: 20%) with 30.5% of small peritumoral alveolar hemorrhage, and 2.9% of major bleeding in 105 patients with tumors to the lung [5], which makes SBRT invasiveness close to one of the RFAs.

We did not make reference to SABR because today the gold standard for lung metastases is surgery when possible. As concluded by Dr Siva in his Journal of Thoracic Oncology Paper in 2010 'There is insufficient evidence to recommend a consensus view for optimal tumor parameters, dose fractionation, and technical delivery of treatment in oligometastatic patient', and such parameters are needed before SABR can be compared with another treatment.

I have no doubt that the future will see decrease in lung surgery for small oligometastatic patients and that low invasive technique will replace surgery in such indication. The optimal technique will have to demonstrate efficacy, tolerance, and cost-effectiveness, even if randomized studies will be difficult as emphasized by early closure of RCTs, trying to compare surgery and SABR in NSCLC (STARS and ROSEL) due to slow accrual R [6].

Primum non nocere

meta-analysis

In their meta-analysis of erythropoietin-stimulating agents (ESA) in patients with breast cancer [1] Aapro et al. found an overall mortality rate of 24.3% in the ESA groups compared with 21.8% in the control groups (as reported in Figure 1A of the manuscript). The associated odds ratio for death is 1.20 with a 95% confidence interval (CI) of 1.03–1.40 [P value (not reported by the authors) = 0.02, calculated with RevMan 5.3]. Moreover, by presentation of sensitivity analyses (i.e. exclusion of the BEST study and presentation of effects of ESA in different settings of breast cancer), the authors try to convince readers that ESAs do not significantly increase the mortality in women with breast cancer. In their abstract, the authors seem to

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