CHAPTER 4

Reduction of airway smooth muscle mass after Bronchial Thermoplasty: are we there yet?

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To the editor,

With interest, we read the letter by Pretolani and colleagues who performed an observational study to investigate the effect of Bronchial Thermoplasty (BT) on airway smooth muscle (ASM) in severe asthma patients (1). Preclinical studies have shown a reduction in ASM after BT that was associated with reduction in airway hyper responsiveness (2). However, the large randomized trials failed to reproduce this effect and showed only moderate clinical improvement in quality of life and exacerbation frequency (3,4). The current study is the first that confirms reduction in ASM in severe asthma patients after BT. The data show quite a dramatic (>45%) decrease in ASM in biopsies of BT-treated airways, and even more surprisingly also in biopsies of the non-BT treated middle lobe. The proposed mechanism is that radio-frequent energy delivered during BT spreads its heat shock effect beyond the airway directly treated. This hypothesis is strengthened by the detection of ground-glass opacities around the non-BT-treated middle lobe in half of the patients. In our opinion the findings described are very important, however great caution should be made in drawing strong conclusions at this moment.

First, the high percentage of radiological abnormalities after BT observed by the French group has never been reported before and is therefore unexpected. We can confirm this observation as in our practice all patients after each BT procedure develop transient radiological abnormalities, mostly segmental atelectasis and/or peribronchial opacities. However, on HRCT made <24 hours after BT, no abnormalities could be detected in the non-BT-treated middle lobe. Second, in the current study ASM mass was analyzed in airway biopsies taken before and after BT at the exactly the same airway carinas and the non-BT-treated middle lobe carina served as a control. Surprisingly, an unexpected decrease in ASM in the middle lobe after BT was observed. It cannot be excluded that (part of) the decrease in ASM detected is simply a scar effect of the prior biopsy. This effect especially applies for the middle lobe since the anatomical area available for biopsies is very limited. In our opinion, this could be a very plausible alternative explanation for the high-level decrease in ASM, also in the non-BT-treated middle lobe. Furthermore, since only a partial decrease in ASM after BT was seen in the earlier lobectomy study (5), it is hard to believe the impact of BT on ASM is this dramatic even in distant located non-BT-treated middle lobe airways. In fact, ideally BT-induced effects on the airway wall are assessed in vivo by a non-invasive technology that has high-spatial resolution over a longer airway section.

Optical Coherence Tomography (OCT), a light-based near-histology high-resolution imaging technology, is a very promising method to fulfill these requirements since individual airway wall layers can be identified and measured longitudinally in an airway stretch in an accurate and reproducible way (6). Therefore, in the TASMA trial (NCT02225392 clinicaltrials.gov), which is a randomized, international multi-
center trial to investigate BT targets, we use OCT, next to airway biopsies and standard X-ray-based imaging, to detect immediate and late effects of BT on airway wall layers, including ASM and link these to clinical outcome. As such we propose that OCT might qualify as an effect and/or screening technology for BT. In line with the above, we fully agree with our French colleagues the importance and need to further unravel BT targets to ultimately improve patient selection for BT.
REFERENCES


