High Z nanoparticles and radiotherapy: a critical view

Authors' reply

We thank Florent Vilotte and colleagues for their comments on our Article;[1] however, the statements are incomplete as presented. First, we believe specifying that "Evidence supports chemical and biological activities of these [high Z] nanoparticles during irradiation, challenging the pure physical radioenhancement concept" is misleading. Each specific nanoparticle has intrinsic properties that determine its efficacy and safety relative to its mode of action. The NBTXR3 nanoparticle, functionalised crystalline hafnium oxide, has been selected among other nanoparticles as a radioenhancer because of the absence of degradation and redox activities.[2]

Second, the mode of action of the NBTXR3 nanoparticle—its capacity to amplify the deposit of energy within tumours when radiotherapy is on, its intratumoral persistence during radiotherapy, and its very good safety when radiotherapy is off—was evidenced through its preclinical[2,3] and early clinical[4] evaluation. We agree that the study validates the mode of action of NBTXR3, given that an increased proportion of patients with a pathological complete response, indicating increased tumour cell death through increased production of free radicals, is a direct sign of efficacy.

Third, we stated that a limitation of our study was the absence of a mock-injected control group because masking was not feasible (radio-opacity), would have put patients under unnecessary risk, and would not have been ethical.[1] Moreover, preclinical antitumour efficacy studies have shown no difference in tumour growth between an intratumoral injection of the control vehicle versus the injection of NBTXR3 in the absence of radiotherapy, whereas enhanced antitumour activity was observed when radiotherapy was introduced where NBTXR3 was present versus the control vehicle.[2]

Finally, because of their size, electron microscopy is the only relevant tool to visualise nanoparticles, which was not available during pathological evaluation. So pathologists were masked when assessing the samples.

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