High Z nanoparticles and radiotherapy: a critical view

We thank Sylvie Bonvalot and colleagues[1] for their study on the use of NBTXR3 in combination with radiotherapy in patients with locally advanced soft-tissue sarcoma. Their results show a significant improvement in pathological complete response (16% *vs* 8%; p=0·044) and R0 resection (84% *vs* 70%; p=0·030) with NBTXR3 in comparison with radiotherapy alone.

We believe the authors probably overstate that this trial "validates the mode of action of this new class of radioenhancer".[1] This conclusion should be taken with caution because any conclusions about the physicobiological postulates underlying the clinical benefit observed in this study cannot be extrapolated from their pathological findings. Moreover, the mode of action of high atomic number (Z) nanoparticles in combination with radiotherapy is highly debated,[2] with a main hypothesis of an increased dose deposit due to higher interactions mediated by direct physical interactions between ionising radiation and nanoparticles (ie, a physical step). Supposing their biological inertia, this would result in no effect without irradiation.[3]

However, the real mode of action of high Z nanoparticles in this combination remains uncertain. Evidence supports chemical and biological activities of these nanoparticles during irradiation, challenging the pure physical radio-enhancement concept and raising the question of their potential toxicity, notably in case of long-term systemic persistency.[4,5]

Another weakness of this study is the absence of an appropriate control group (eg, injection of solution without NBTXR3); hence, it is difficult to impute the observed effects only to the NBTXR3 nanoparticles rather than intratumoral injection process (10% of tumoral volume, up to 40 needles). In addition, the masking status of the pathologist assessment is not clearly stated, but could be of importance for reporting a comparative study on the basis of pathological response. Indeed, the possibility for the pathologist to visualise nanoparticles by microscopic evaluation is not addressed.

Nanomedicine is a promising new therapeutic area. Bonvalot and colleagues' study provides additional evidence that nanoparticles are an interesting new tool in cancer treatment; however, the mechanism of action of these hafnium nanoparticles when combined with radiotherapy is not clearly understood, and requires further study.

We declare no competing interests.

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