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Ionoacoustic treatment monitoring for radiosensitizer-enhanced carbon ion therapy: a feasibility study

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Purpose

To evaluate the impact of radiosensitizers on ion-induced acoustic emissions (ionoacoustics) and assess the accuracy of ionoacoustic range verification for carbon ion therapy at clinical synchrotrons.

Methods

Acoustic emission resulting from the absorption of optical photons produced from scintillation and absorbed in optical dyes or photosensitizers (similar to photodynamic therapy) were investigated. Alternatively, the local enhancement of the energy deposition in presence of gold nanoparticles (radiosensitizers) was also evaluated. FLUKA Monte Carlo simulations were performed to model a monoenergetic carbon ion beams (215 MeV/u) in water in presence of scintillation materials or gold nanoparticles. The resulting acoustic emission was simulated using k-Wave, considering the temporal microstructures of carbon ions delivered by synchrotrons. The interference pattern (beats) between the direct ionoacoustic signal from the Bragg peak (BP) and the pressure produced due to radiosensitizers at the location where the ion beam enters the targeted volume was analyzed in the frequency domain. The BP position relative to the tumor entrance was estimated from the beat frequency accounting for the speed-of-sound in the target.

Results

Assuming sufficiently high light yield in the typical range of scintillation decay time, the absorption of optical photons as used in photodynamic therapy can enhance the ionoacoustic emission, e.g., light emission at wavelength of 300 nm with a light yield of 103 photons/MeV increases the signal amplitude by 50%. Alternatively, low concentration (<1wt.%) of high-density materials like gold nanoparticles significantly enhance the ionoacoustic emission (>100 % increase). The additional pressure generated at the entrance of the target in presence of radiosensitizers allows for accurate BP localization (<1% error relative to the 9.8 cm range) for ion beam at synchrotrons.

Conclusion

This simulation study shows the potential benefit of radiosensitizers on ionoacoustics-based range verification to enable accurate BP localization for carbon ion beams delivered by synchrotron accelerators.

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Supplementary information

Context: Targeted therapeutic agents such as radiosensitizers or photosensitizers in combination with scintillation materials aim to locally enhance the dose or singlet oxygen production, both improving the tumor cell death.

Innovation/impact: This study investigates for the first time the influence of these agents on the ionoacoustic emission in the context of carbon ion therapy. Moreover, ionoacoustics is currently restricted to pulsed ion beams, e.g., μs pulse delivered from synchro-cyclotrons. Our results show that ionoacoustics can also be used at synchrotron-based clinical facilities (continuous beam delivery with a MHz microstructure) using such agents.

Key results: Radiosensitizers localized in the targeted volume result in an additional energy gradient (e.g., at 90 mm on [Figure 1](#)) leading to secondary acoustic emissions. The interference induced by the secondary emissions allows retrieving the BP for a continuous ion beam. The optical photon absorption increases the amplitude of the direct signal ([Figure 2](#)) and allows for sub-millimeter BP localization accuracy (error < 1%, see [Figure 3](#)). Alternatively, the pressure and localization accuracy can be improved by using high-density radiosensitizer nanoparticles, as those currently used in ion therapy (e.g., gold nanoparticles, [Figure 4](#)). The impact of the ion beam energy and heterogeneities on the acoustic signal remain to be assessed, as well as the detectability of the still very low-pressure amplitudes (< 1mPa at synchrotrons compared to 10-100 mPa for pulsed beams) considering realistic detector sensitivity and frequency response.

