Improved performance with new single particle localization algorithm for ultrasound localization microscopy *in silico* and *in vivo*

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Background, Motivation and Objective

Ultrasound localization microscopy (ULM) has been demonstrated to overcome the penetration/resolution paradigm [Couture *et al*, 2018]. It relies on localizing the centre of a single microbubble and accumulating a large number of echoes to produce micrometric images of *in vitro* canals in 2D [Couture *et al*., 2011, Viessman *et al,* PMB, 2013], 3D [Desailly *et al,* 2013, Heiles *et al*, 2019] and *in vivo*, rat brain microvasculature [Errico *et al,* 2015, Heiles *et al*, 2018], tumours [Lin *et al*, 2017]. In this study, we aim to compare the performance of algorithms used for ULM and introduce a new method based on radial symmetry of the system's point spread function.

Statement of Contribution/Methods

We first simulated radiofrequency and beamformed images of a moving microbubble in a 20 x 9.6 x 9.6 mm^3 volume insonified with 12 tilted 2D plane waves at 9MHz using Verasonics simulation and added speckle noise. The microbubble was moved in all possible directions with l /10 increments yielding 1331 cases. The algorithms were also tested on *in-vivo* ULM data of the craniotomized rat brain obtained after the IV injection of 0.2 mL of Sonovue (Bracco®) [Hingot *et al.* 2019]. Either a 15 MHz probe (Vermon, France) - 20V, 3 titled plane waves, framerate = 1kHz - or a 2D matrix array (Vermon, France) were used to acquire in between 75k to 200k images/volumes. The new algorithm relies on the radial symmetry of the PSF about its centre. By minimizing the distance from an initial guess of the center to the lines directed by the computed intensity gradient, it is able to localize the center of the bubble. It was compared in 2D and 3D with approaches found in the literature (3 different interpolations, 3 different weighted averages).

Results/Discussion

We calculated mean and standard deviation of absolute errors on z, x and y axis, as well as the root mean square error (RMSE) for *in silico* tests with -15dB gaussian noise (figure 1). The new radial symmetry method has the lowest RMSE (5.8E-2 λ) and the lowest x-error (3.4E-2 λ), while interpolation based method have the lowest z-error (4.0E-2 λ). However the computation times for interpolation are 20 fold compared to radial symmetry in 2D, making their translation in 3D challenging. On ULM images of the rat brain, radial symmetry reduces the aliasing effect often observed in ULM. Hence, this new approach improves the subwavelength tracking of microbubbles, both in direction and velocity.

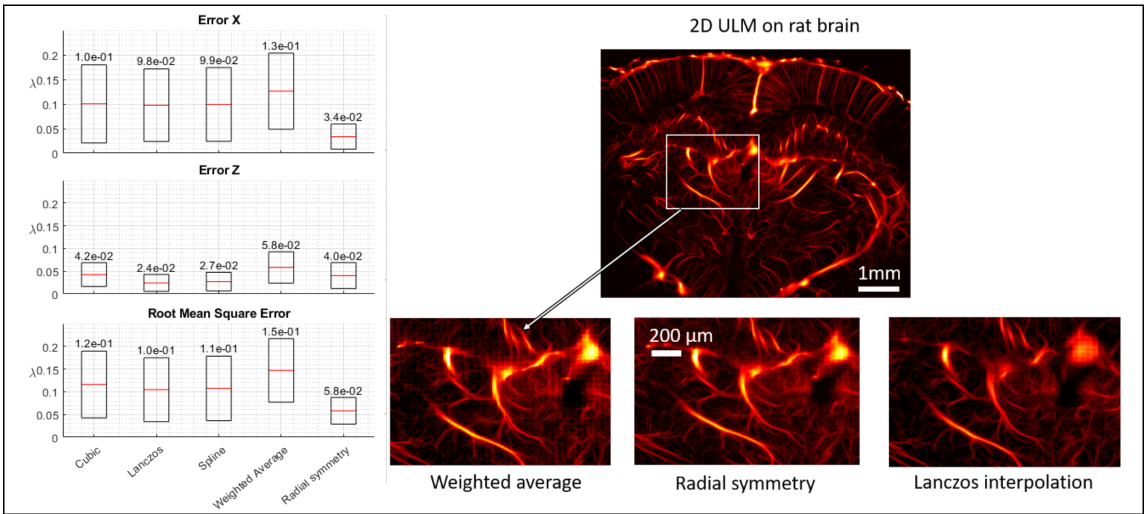

Figure 1. Errors on in silico cases and comparison of image quality on in vivo cases