Predicting tumour responsiveness to chemotherapy in volumetric liver ultrasound images

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Liver tumours

Approximately 40,000 patients are diagnosed each year with either primary or secondary liver cancers in the UK. Curative surgery is only suitable in 10-25%, with chemotherapy forming the mainstay of treatment. In order to achieve sustained therapeutic effect whilst minimising drug toxicity, this is usually given at regular time intervals according to a clinically prescribed treatment schedule.

Tumour response to chemotherapy

Since only one third of patients respond to treatment, it would be advantageous if clinicians can detect non-responders early during a course of treatment, and potentially offer salvage therapy to these patients.

Liver tissue characterisation

Medical ultrasound images can be analysed either by characterising the local spectrum or the envelope distribution of the backscattered signal. In this work, we focus on the latter by modelling it with a Nakagami distribution for its capability to represent the various backscattering conditions from image texture. Fig. 1 shows the capability of the Nakagami distribution to model different scattering conditions related to Rayleigh distribution.

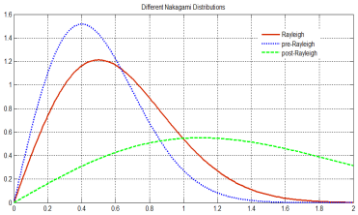

Figure 1: Varying the Nakagami probability density function shape (μ) while fixing the scale parameter (ω) to 1 in order to represent pre-Rayleigh ($\mu < 0.5$), Rayleigh ($0.5 \leq \mu \leq 1$), and post-Rayleigh or Rician ($\mu > 1$) distributions.

3D Ultrasound liver tumour volume acquisition

Conventional B-mode and radiofrequency ultrasound data were acquired using a diagnostic ultrasound system (z.one, Zonare Medical Systems) with a L14-5w linear array mounted on a manual positioning system. Cross sectional images of xenograft tumours in mice were obtained with 1mm step-wise movement of the array until the whole tumour volume was imaged (Fig. 2). Manual segmentation of each image were performed prior to processing in a pixel per pixel based approach. The Nakagami distribution was fitted to the distributions in each sliding-window and parametric images were generated (Fig. 3).

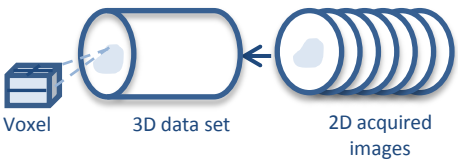

Figure 2: Image acquisition using step-wise acquisition of tumour cross section to form 3D image of the tumour volume.

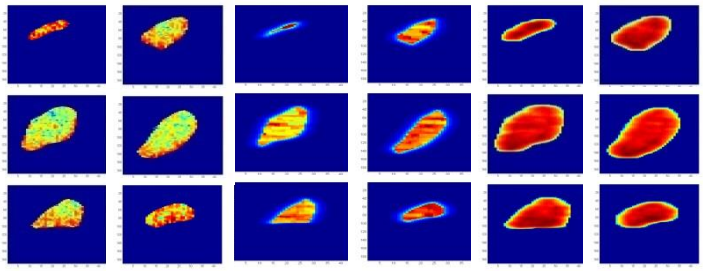

Figure 3: Six ultrasound B-mode slices representing a segmented liver tumour volume. From left to right: a) intensity images and corresponding b) shape and c) scale (energy) Nakagami parametric images.

Nakagami parametric voxel-based formation

The Nakagami distribution $N(x)$ – which is equivalent to a scaled square root of a Gamma distribution - has the density function

$$N(x) = 2\left(\frac{\mu}{\omega}\right)^{\mu} \frac{1}{\Gamma(\mu)} x^{(2\mu-1)} e^{-\frac{\mu}{\omega}x^2}$$

where x is the log-compressed envelope of the signal, with the shape of the distribution defined by the μ parameter and the local backscattered energy represented by the scale parameter $\omega > 0$, for $x > 0$. The Nakagami parameters are generally estimated by the 2nd and 4th order moments as:

$$\omega = E(x^2), \qquad \text{and} \quad \mu = \frac{[E(x^2)]^2}{Var(x^2)} = \frac{[E(x^2)]^2}{E(x^4) - [E(x^2)]^2}$$

Results

28 mice were randomised into 4 treatment groups : a) Phosphate buffer solution, control (n=6), b) Thermosensitve liposome encapsulated Doxorubicin, partial treatment (8) , c) Hyperthermia with high intensity focused ultrasound, partial treatment (6), and d) combination of b] and c] treatment regimes, full treatment (8). % of pixels in each tumour volume with pre-Rayleigh distributions were calculated, and the mean change from baseline was compared across treatment groups using ANOVA. A statistically significant difference was found between the 4 treatment groups ($p = 0.05$). This is most marked between group a) (-20.4%) and d) (-6.5%) representing the control and full treatment group respectively.

Conclusion

Voxel-based Nakagami parametric tumour region analysis at different time points throughout chemotherapy treatment provide potential indicators of early tumour response to treatment. This may help clinicians to optimise administration of chemotherapy treatment in future.

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