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Comparison of MR and ultrasound thermometry for monitoring tissue temperature during hyperthermia

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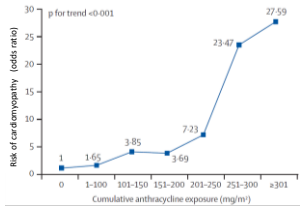
Applying localized drug delivery to pediatric cancer

Doxorubicin is used for the treatment of vast majority of sarcomas

Local control is critically important in sarcoma

Augmenting the local effect of treatment may increase the ability to deliver or reduce the toxicity of local control.



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Armenian et al, Lancet Oncology Mar 2015

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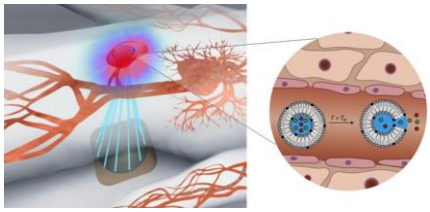
Hyperthermia mediated drug delivery



Thermosensitive liposomes containing doxorubicin (i.e. Thermodox)

Stable for 1-2 hours in bloodstream,

Rapidly release drug when passing through tissue heated above 41°C,

Prolonged heating allows continuous release for enhanced cellular uptake.

New Thermodox Phase II, III trials for breast, liver enrolling, HIFU trials planned.

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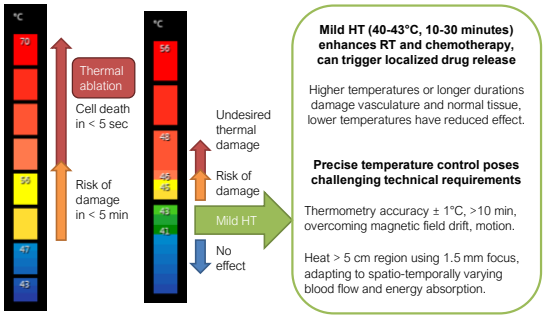
Benefits and challenges of mild hyperthermia



Mild HT (40-43°C, 10-30 minutes) enhances RT and chemotherapy, can trigger localized drug release

Higher temperatures or longer durations damage vasculature and normal tissue, lower temperatures have reduced effect.

Precise temperature control poses challenging technical requirements

Thermometry accuracy ± 1°C, >10 min, overcoming magnetic field drift, motion.

Heat > 5 cm region using 1.5 mm focus, adapting to spatio-temporally varying blood flow and energy absorption.

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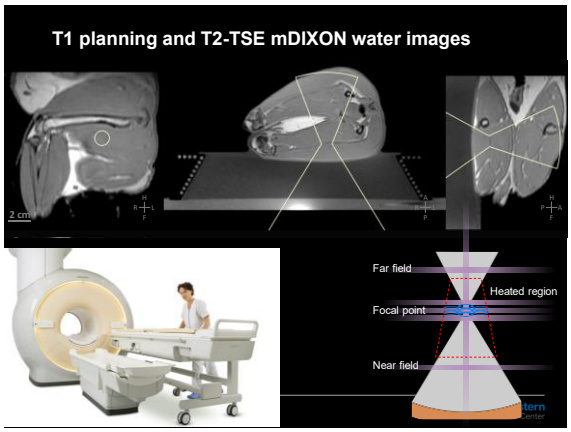
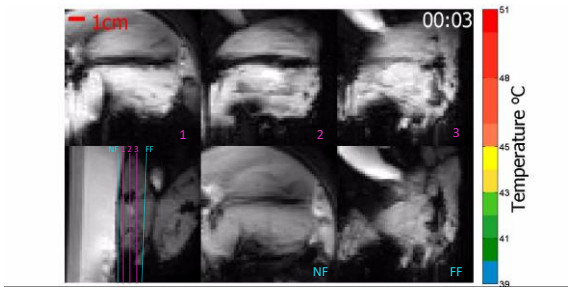
T1 planning and T2-TSE mDIXON water images



MR-HIFU hyperthermia in rabbit tumor



Temperature in 10 mm diameter region kept at 42°C for 40 minutes (1.2 MHz, 60W).
Temperature-sensitive liposomal doxorubicin infused during first 6 minutes.

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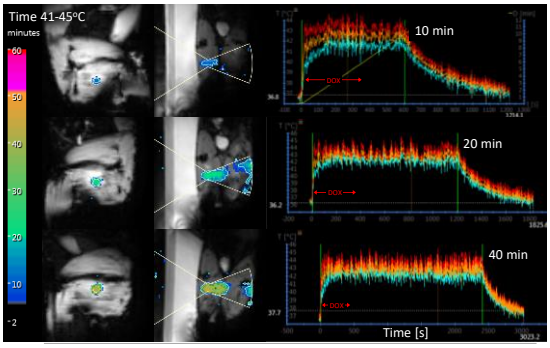
Heating results: 10, 20, and 40 minutes



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Importance of drift correction for long duration heating

- Type of correction used for PRF shift thermometry matters
- Validation required on every platform due to hardware differences

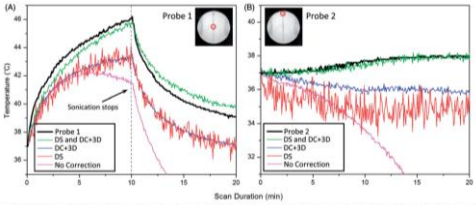

Figure 8. Comparison is made between fibre-optic measurements and MR thermometry using various drift correction strategies: raw data (No Correction) dynamic stabilisation only (DS), DC = 3D drift correction algorithm only (DC = 3D), and combined strategy (DS and DC = 3D). The drift correction algorithm validated here is the combination of DC drift correction and 3D first order drift correction. Panels A and B represent data acquired at probe 1 and probe 2 (shown in the insert), representing the heated and unheated region, respectively.

Bing et al, International Journal of Hyperthermia, 32(6), 2016

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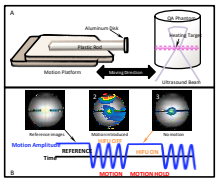
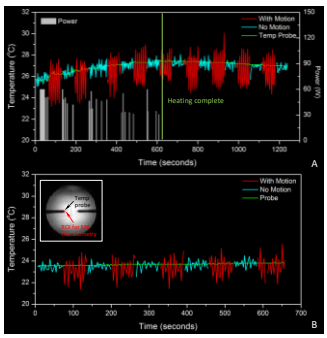
Strategies for dealing with respiratory artifacts

- PRF shift thermometry extremely sensitive to motion and Bo disturbances
- A strategy of ventilated breath-holds might be a strategy to achieve long duration heating





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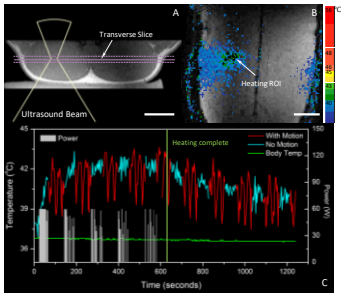

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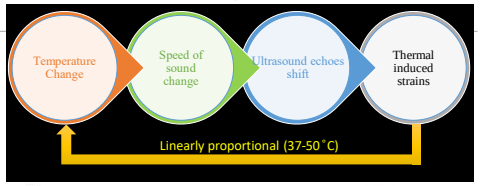
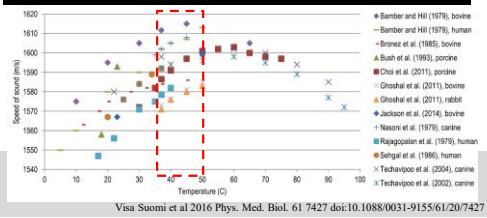
Strain-based US thermometry





Visa Suomi et al 2016 Phys. Med. Biol. 61 7427 doi:10.1088/0031-9155/61/20/7427

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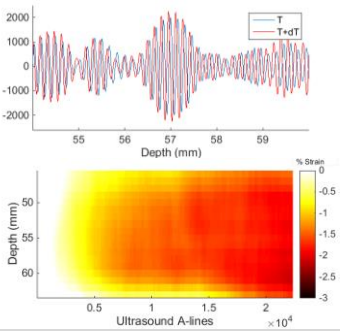
US signal analysis

US echo shift

US thermal strain (M-mode)



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Question

Is US thermometry feasible for mild hyperthermia in vivo?

Two methods to validate US thermometry

- MR thermometry (PRF shift)
- Gold-standard implanted fiber-optic temperature sensor

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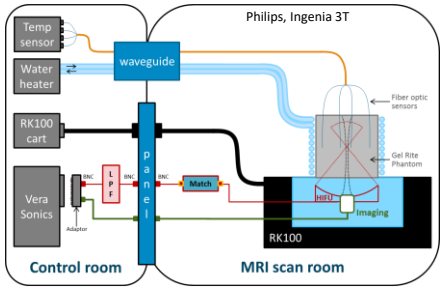
Ex vivo calibration experiment setup



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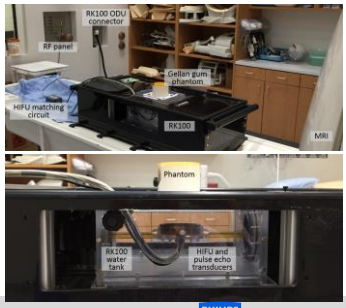
Ex vivo calibration experiment setup



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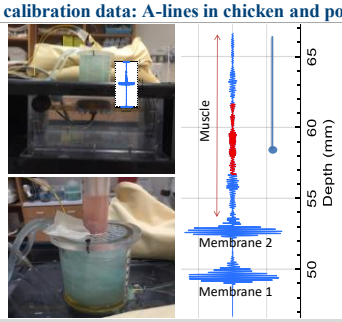
Ex vivo calibration data: A-lines in chicken and pork muscle



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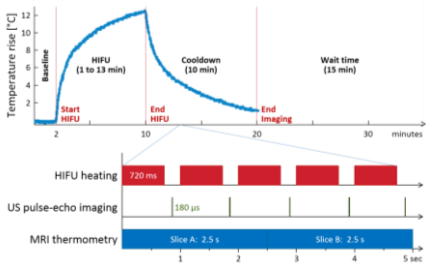
Timing of interleaved HIFU and pulse-echo acquisition



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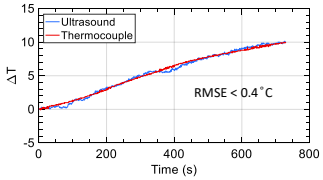
Ultrasound vs Fiber-optic sensor (35-45 ℃)

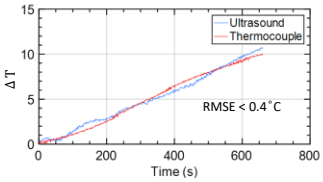
Chicken muscle

Strain to T conversion coefficient:
$-4.98 \pm 1.0*10^{-4}$ / ℃



Pork muscle

Strain to T coefficient:
$-4.70 \pm 0.8*10^{-4}$ ℃



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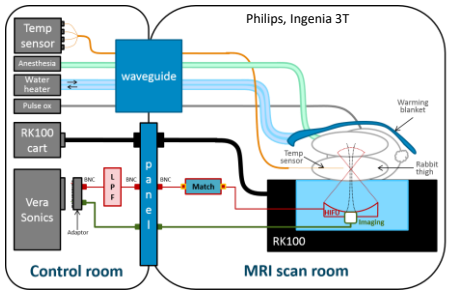
In vivo Experiment setup (Rabbit n=4)



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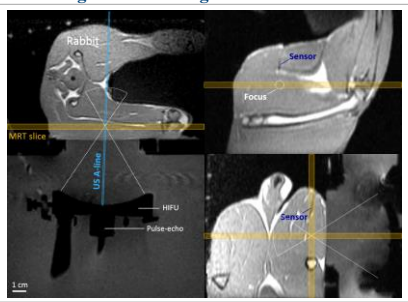
3D T1-weighted MRI images



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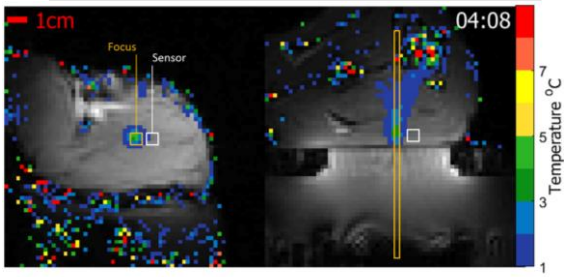
Results: MR vs fiber-optic sensor



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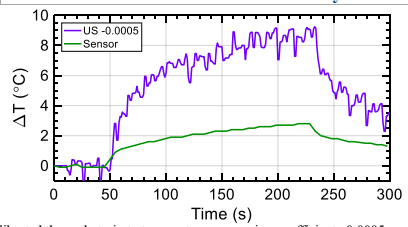
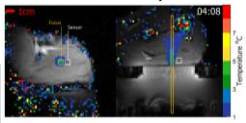
Results: US at focus vs sensor 4 mm away from focus



Calibrated thermal strain to temperature conversion coefficient -0.0005 was applied.



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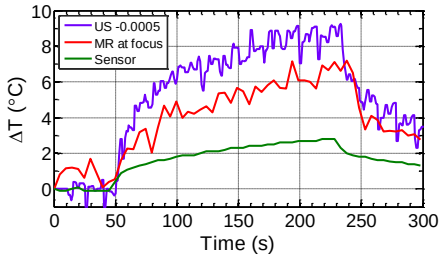
Results: US vs MR vs Fiber-optic sensor



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Conclusion

- Ex vivo ultrasound thermometry has been successfully performed in both chicken and pork muscle by comparing with implanted fiber-optic temperature sensors.
- Simultaneous MR and US thermometry were successfully acquired in stationary in vivo rabbit muscle under regular respiration and perfusion. In comparison with implanted fiber-optic sensor readings, we showed that strain-based ultrasound thermometry is feasible in the mild hyperthermia range.
- Although effective, the calibrated strain-to-temperature conversion coefficient has to be validated in more experiment conditions and more types of tissues.

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Acknowledgement

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