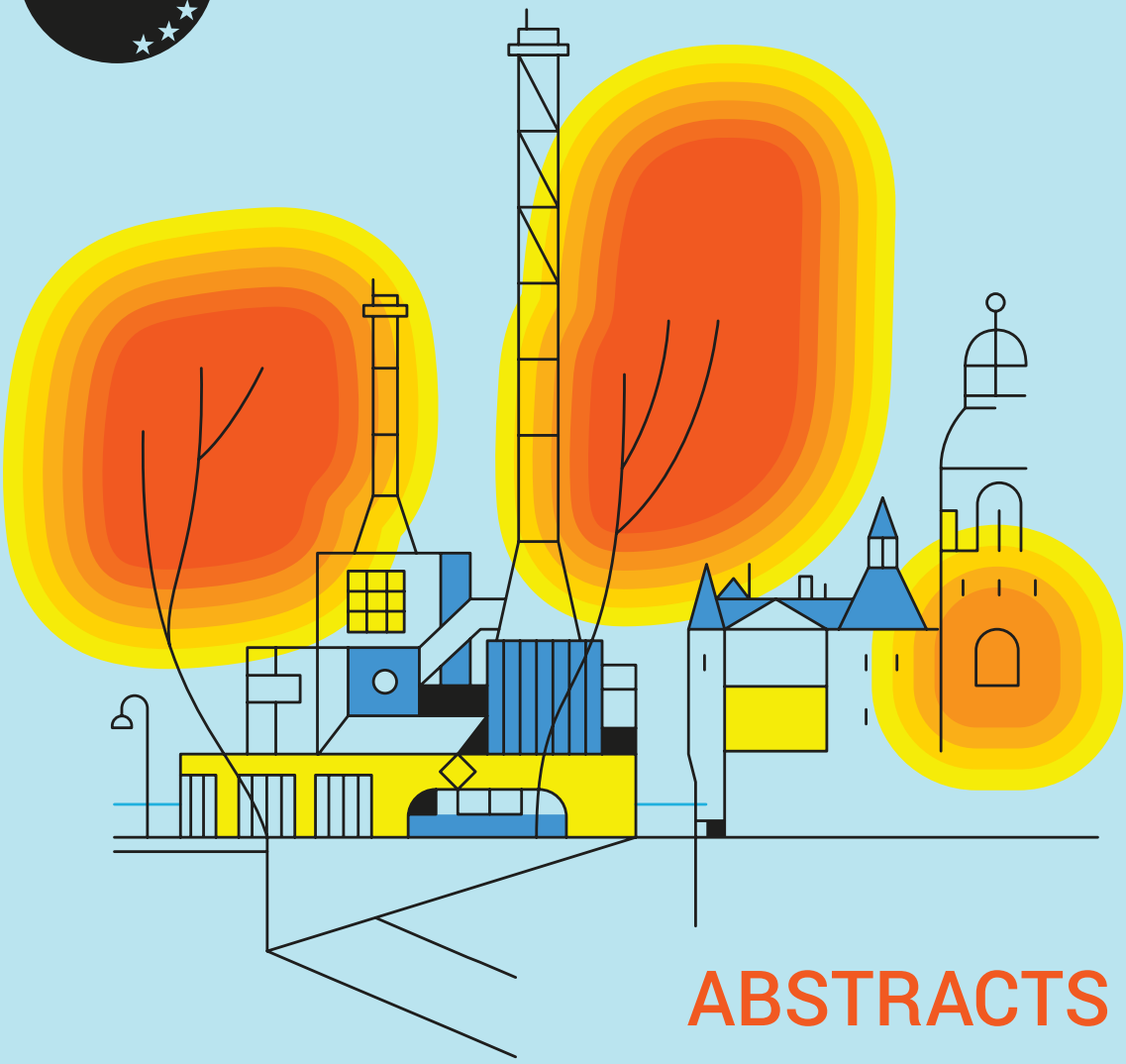


ABSTRACTS

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bronchoscopy system under CBCT guidance and monitoring offers potential for effective and consistent MWA treatment of lung nodules.

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An *in vitro* system for focused ultrasound hyperthermia (and radiotherapy) studies using spheroids

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Introduction

Ultrasound can be used for clinical hyperthermia. *In vitro* studies are challenging as acoustic interactions in 2D cell suspensions are not representative of those *in vivo*. The lack of absorption in culture medium means acoustically induced thermal effects are absent. A system for ultrasound (US) hyperthermia studies (+/- radiotherapy (RT)) of 3D *in vitro* models, with thermal dosimetric control has been built with the aim of improving prediction of *in vivo* outcomes.

Material and methods

Acoustic holography was used to design a lens that widened and shortened the focal region of a 64 mm diameter (F-no=1) 1.66 MHz ultrasound transducer (H148MR Sonic Concepts, USA) from 2 mm diameter by 12 mm to 6 mm x 8 mm wide by 8 mm on axis.

For exposure, U87MG glioma spheroids were held in a two-part ultrasound-absorbing biocompatible gel (IEC standard tissue mimic + 1% phenol red). The lower half had 25 or 100µm diameter T-type thermocouples (TCs) mounted with their junctions within 0.5 mm of the bottom of each of three 1 mm diameter, 0.7 mm deep dimples spaced 2 mm apart. The top, flat, 4 mm thick, gel fitted within the 3D printed frame holding the first part.

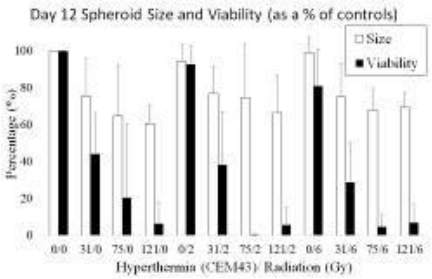
One spheroid was pipetted into each dimple before sealing with Matrigel. Medium was used to couple the gel lid to its base and the ensemble placed in a 38oC water tank. After equilibrating, real-time temperature and thermal dose monitored US was delivered until the central spheroid received 119.5 CEM43. The thermal dose in the other wells was ~30 and 75 CEM43. Controls were sham-exposed simultaneously in the same water bath. Spheroids were exposed to 0, 2 or 6 Gy RT (Xstrahl Cell irradiator) 0 to 6h later. Spheroid size (Celigo Imaging cytometer) and viability (Cell Titer Glo 3D assay) were measured on day 12.

Results

Of 117 US exposed spheroids, 110 were successfully harvested. 121 (n=39), 75 (n=35) and 31 (n=36) CEM43 were delivered (standard deviations 1, 11 & 23% respectively). RT alone had little effect. US alone (>= 31 CEM43) resulted in <50% viability but with less effect on spheroid size, while US+RT enhanced viability loss to <10%.

Conclusion: The exposure system works well, with 94% spheroid harvest possible, and clinically relevant thermal doses being achievable. Comparison of viability and size data suggests the latter to be a poor indicator of cellular response. 75 & 121 CEM43 had similar effects. The combination of HT+RT resulted in greater loss of viability than either alone.

Fig. 1



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Heating power of dual-material radioactive magnetic nanoparticles for thermo-brachytherapy

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INTRODUCTION: Magnetic nanoparticles (MNP) are known to generate heat in alternating magnetic fields of a frequency that does not interact with tissue. With this method, it is possible to selectively heat tumor tissue loaded with MNP, while the surrounding healthy tissue remains at body temperature. When the MNP have sufficient heating power, i.e. have strong interaction with the magnetic field, it is possible to reach thermal ablation temperatures within the tumor. By combining these magnetic properties with radioactivity, thermo-brachytherapy can be delivered in one treatment. As a first step, dual-material radioactive magnetic nanoparticles were developed and their heating power measured.

MATERIALS & METHODS: The specific loss power (SLP), i.e. heating power, of a series of the novel, hybrid MNP was measured using Magnetherm Digital device with frequencies ranging from 50 kHz to 750 kHz and field strengths of 15 to 30 mT. Magnetic properties of the hybrid MNP were evaluated using superconducting quantum interference device (SQUID) magnetometer measuring saturation magnetization (Ms) as a function of magnetic field (H).

RESULTS & DISCUSSION: Hybrid nanoparticles with a core of palladium, which will serve as the radioactive source using 103Pd, and with a magnetic shell of iron-oxide were synthesized. By varying the synthetic conditions, hybrid MNP in different sizes, shapes, and magnetic properties are obtained. As reference the SLP of the hybrid MNP are compared to the SLP of commercial iron-oxide MNP using the same experimental setups. The obtained SLP values for the hybrid MNP"s ranged from 0 to 225 W/g. Some samples were not stable in suspension and aggregated, which resulted in reduced or even no heating power. Samples with high saturation magnetization, normally showed larger SLP, however SLP values of such samples were significantly reduced upon aggregation. The stability is mostly dependent on the surface functionalization of the nanoparticles. When stable in solution, the MNP with a higher Fe/Pd ratio showed larger SLP.

CONCLUSION: Hybrid MNP with a non-magnetic core can be synthesized reaching SLP values up to 225 W/g, with SLP values increasing with larger Fe/Pd ratio and larger Ms. This SLP is expected to be sufficient for thermal ablation of tumors as small as 15 mL with 1mg/mL MNPs in the tumor and as small as 1mL tumor volumes using 5mg/mL dosis.

Acknowledgment: Research funded by NWO-TTW, Project 16238 NP-thermobrachy