N-isopropylacrylamide (PNTPA) is a thermosensitive polymer that shrinks bleeding and malignancy is quite exclusively observed in tumors. A dual therapy of targeted hyperthermia and cytotoxic killing of HCC was applied for 800sec, temperature of the TONP solution rose from 20°C to 43°C. When MF is applied, IONP respond by generating heat. Polyacrylamide-coated-IONPs are subjected to a MF (3) doxorubicin is released in a controlled fashion when solution of doxorubicin-loaded-polymer-coated-IONP. When PNTPA-coated-TONP are exposed to a MF generated by MRI, dual therapeutic modalities of hyperthermia and cytotoxic chemotherapy are possible.

Aims: To show (1) drug-loaded-polymer-coated-IONP can be delivered intra-arterially and localized to human hepatocellular carcinoma (HCC) in a rat model (2) heat is generated when the doxorubicin-loaded-polymer-coated-IONPs are subjected to a MF (3) doxorubicin is released in a controlled fashion when solution of doxorubicin-loaded-polymer-coated-IONP is heated.

Methods: Morris 7777 hepatoma cell lines are implanted into the liver of buffalo rats. Two weeks later, baseline MRI is done to document development of HCC. 0.5ml of doxorubicin-loaded-polymer-coated-IONP solution is injected into the hepatic artery and MRI performed to confirm localization. The rats are then sacrificed and histology obtained from the liver, stomach, kidney, spleen and lung. The doxorubicin-loaded-polymer-coated-IONP solution is subjected to a MF and the temperature of the solution is measured to demonstrate heat effect. The concentration of doxorubicin released is measured by spectrophotometry.

Results: The IONP solution was successfully delivered via intra-arterial injection. Post-injection MRI scans confirmed the localization of IONP in HCC. Iron particles were seen on H&E stain in tumor tissue but not in normal liver or in other organs. When an alternating MF (0.8 tesla) was applied for 800sec, temperature of the IONP solution rose from 20°C to 43°C. When doxorubicin-loaded-polymer-coated IONP solution was subjected to the MF, dual-therapy effect was witnessed: temperature increased from 32°C to 48°C, during which 4.6% by weight of bound doxorubicin was released.

Conclusions: We have demonstrated in a rat model for the first time the feasibility of using doxorubicin-loaded-polymer-coated-IONP for synergistic dual therapy of targeted hyperthermia and cytotoxic killing of HCC.