Boosting the Chemotherapeutic Effect of Cancer Drugs using Focused Ultrasound (FUS)

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Many types of drug molecules bind to blood plasma proteins such as albumin and alpha 1-acid glycoproteins. This binding is rapidly reversible and occurs through weak (on the order of piconewtons) molecular-level interactions. When binding occurs, the resulting drug-protein complexes are sequestered in the bloodstream, profoundly reducing effective drug delivery. One potential solution to improve drug delivery is to increase the systemic dose. However, this approach has drawbacks for chemotherapy agents, where higher doses are often associated with serious side effects. This warrants a new technique that can increase the unbound concentration of a chemotherapy drug with spatial selectivity in order to isolate the effect to the targeted tumor mass. Research has shown that low-intensity focused ultrasound (FUS) produces nonionizing mechanical radiation forces that can temporarily disrupt plasma protein binding (PPB), locally increasing unbound drug concentration. Using a murine xenograft model, we applied this technique to unbind cisplatin, a chemotherapy drug that binds to albumin at a rate of over 95%, in order to examine if FUS can enhance the delivery of unbound cisplatin to cervical cancer and thus boost treatment efficacy. We found that a combination of cisplatin and FUS caused a significant reduction in tumor volume compared to the use of cisplatin alone. This study provides the first evidence that FUS offers unprecedented improvements in the non-invasive enhancement of chemotherapeutic agents with high PPB. This technique may allow for the use of lower systemic doses (and thus reduced side effects) to yield equivalent treatment outcomes.