Mechanical Interventions to Improve Drug Uptake and Delivery to Metastatic Breast Cancer in Bone

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INTRODUCTION:

Bone metastasis is the devastating end-stage of cancer where the disease has spread from the primary site to bone. Prevalent in breast and prostate cancers, bone metastases are commonly treated using systemic administration of chemotherapeutic agents. Due to morphological changes in the tumor microenvironment and elevated interstitial fluid pressure, tissue penetration of therapeutic agents is often more limited in cancerous tumors compared to normal tissue. To overcome this limitation, we propose a novel approach to use non-invasive mechanical loading to increase the molecular transport of drugs into bone tumors.

METHODS:

In this pilot study, nine 12-13-week-old female RNU nude rats (175-225g) were injected in the right proximal tibia with MDA-MB-231-Luc (luciferase-expressing human metastatic breast cancer cells; $1.25\text{-}2.5\text{x}10^6$ cells in 25 µL of serum-free medium) using an IACUC-approved protocol. With this preclinical model, cells were allowed to grow for 1-2 weeks before the uptake of ^{18}F-sodium fluoride (^{18}F-NaF, 37±7 MBq) was measured within the tumor. *In vivo* micro-PET/CT imaging was used to assess tracer uptake in the tumor region before and after walking on a treadmill (n=4) for 10 min at a speed of 5 m/min or standing on a vibrating platform (35Hz, 0.3g peak, n=5) for 10 min. The maximum percent of tracer injected dose per unit volume (%ID/mL) was calculated from right (tumor-bearing) and contralateral (control) left tibial metaphysis volumes of interest.

RESULTS:

^{18}F-NaF uptake was significantly higher in the right, tumor-bearing tibia after treadmill exercise. Full body vibration showed an increasing yet non-significant %ID/mL trend in the tumor-bearing tibia.

DISCUSSION AND CONCLUSION:

This pilot study demonstrates that treadmill walking and vibration have the potential to amplify drug delivery to tumors, and further studies are underway to more fully assess the utilization of these approaches. For patients with bone metastases, clinical usage of noninvasive mechanical interventions is a treatment strategy that may enhance uptake and therapeutic effect of drugs while potentially decreasing systemic drug dosage and unwanted side effects.