

Heart-Generated Mechanical Stimuli as an innovative Cancer Therapy

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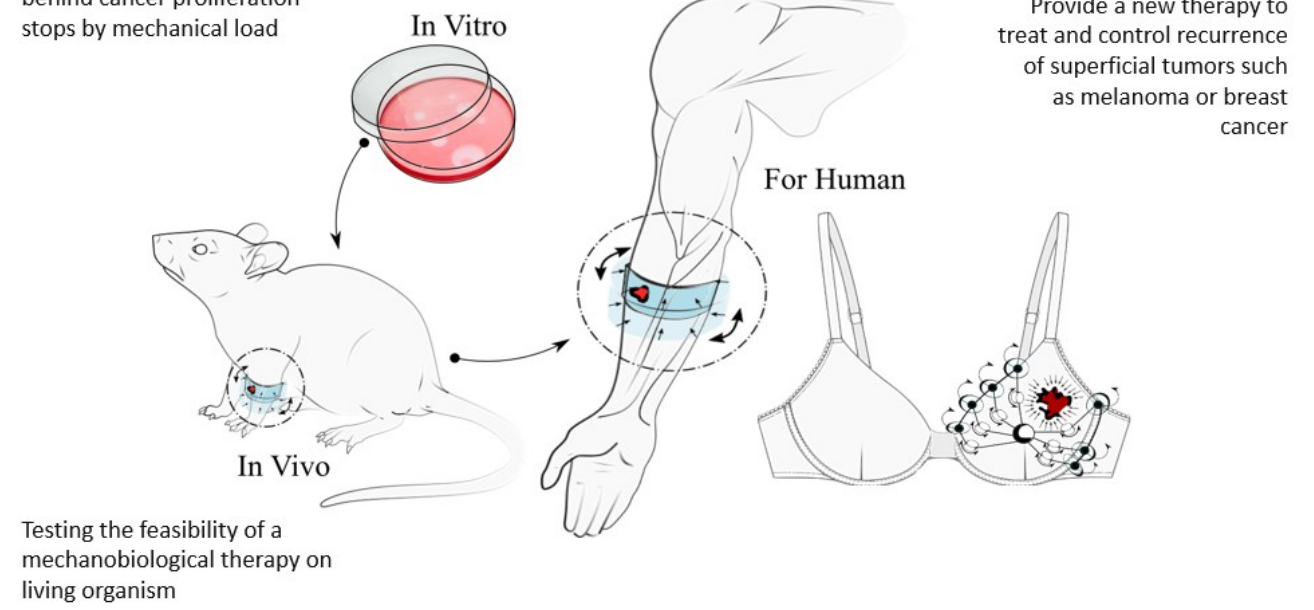
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BACKGROUND AND AIMS

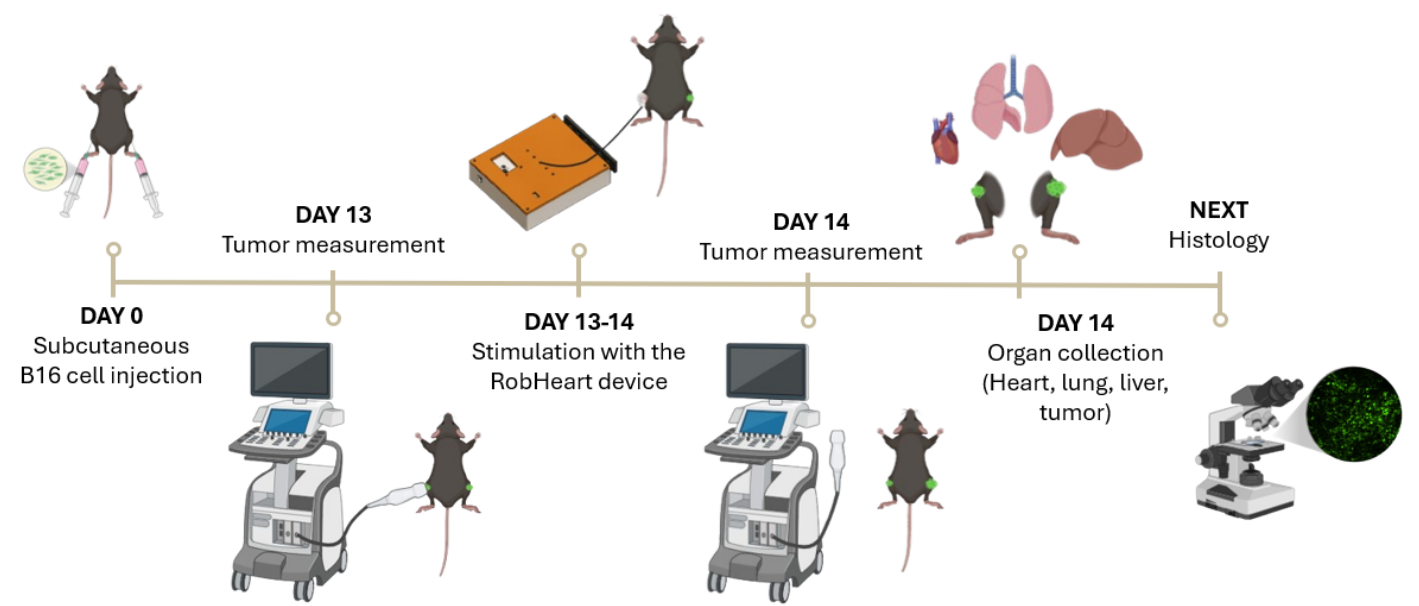
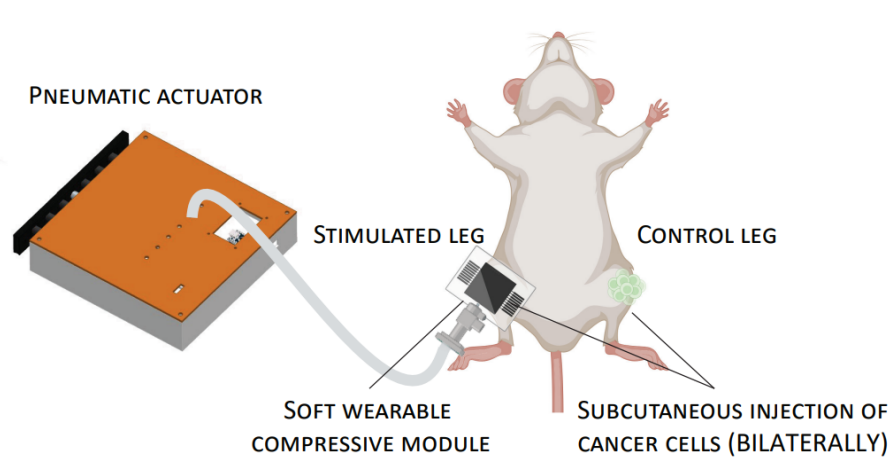
- Cardiomyocytes (CMs) actively divide during embryonic development, whereas the adult mammalian heart retains a limited regenerative potential^{1,2}. Among the mechanisms potentially responsible for the loss of CM proliferative capacity CM at birth is a sudden increase in mechanical load.
- Primary cardiac tumors are rare, with a reported prevalence of 0.0017-0.028%³.
- Cardiac metastases are also rare, with a post-mortem incidence of 1.5–20% in cancer patients⁴.
- Mechanical forces from cardiomyocyte contraction and pressure/volume load suppress the growth of tumor cells engrafted in the myocardium, contributing to the heart's resistance to cancer⁵.

Dissecting the genetic and biological mechanism behind cancer proliferation stops by mechanical load



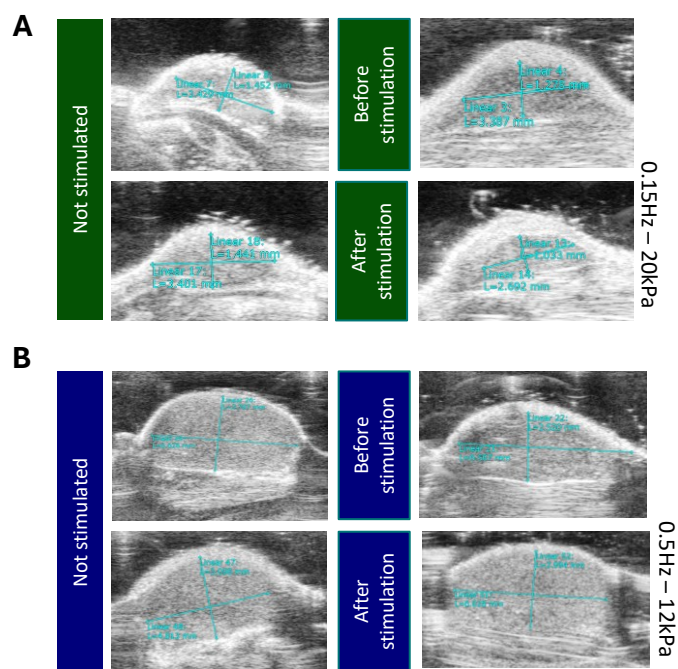
METHODS

RobHeart: a wearable soft robotic device for cardiac-like mechanical stimulation

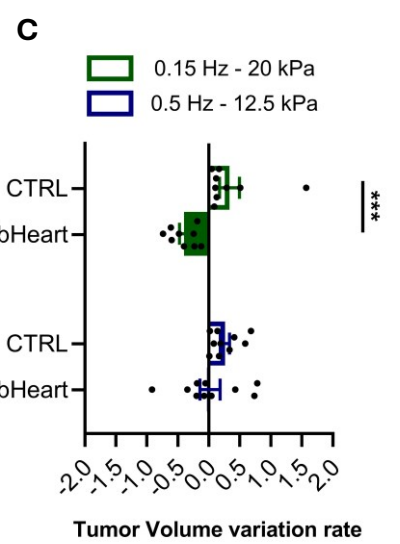


RESULTS

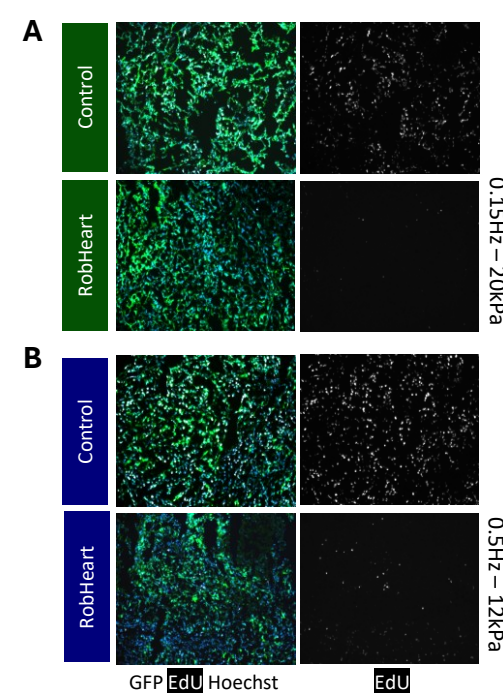
Cyclic mechanical stimulation reduces tumour growth



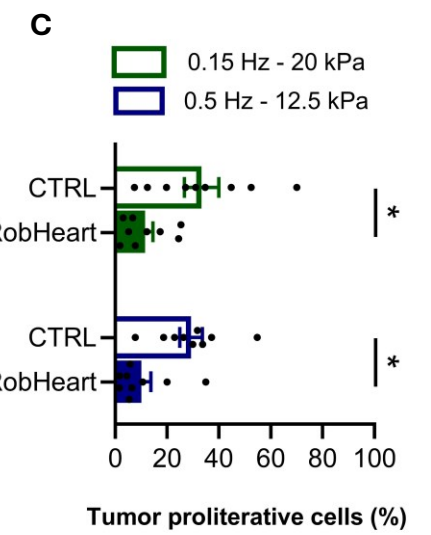
A-B. Ultrasound images of tumor masses. C. Tumor volume variation rate (VR) under cyclic mechanical stimulation of subcutaneous melanoma at different frequencies and intensities



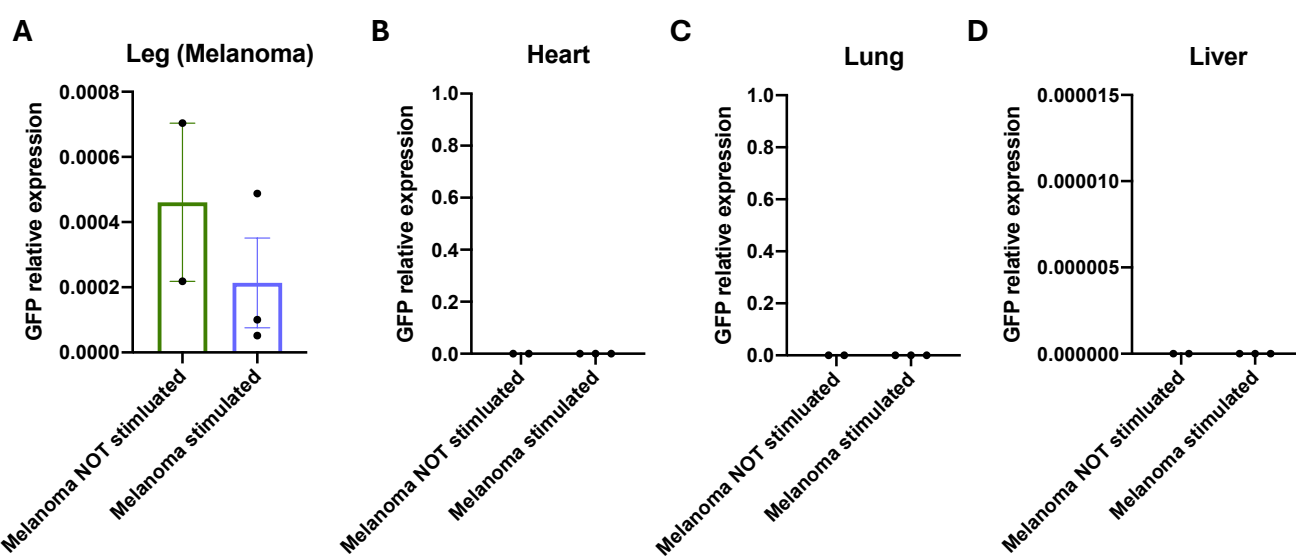
Cyclic mechanical stimulation inhibits tumor cell proliferation



A-B. Immunofluorescence of GFP+ melanoma tumor masses stained for EdU under different mechanical stimulation conditions. C. Quantification of total and proliferating tumor cells across stimulation parameters (0.15 Hz – 20 kPa and 0.5 Hz – 12.5 kPa).

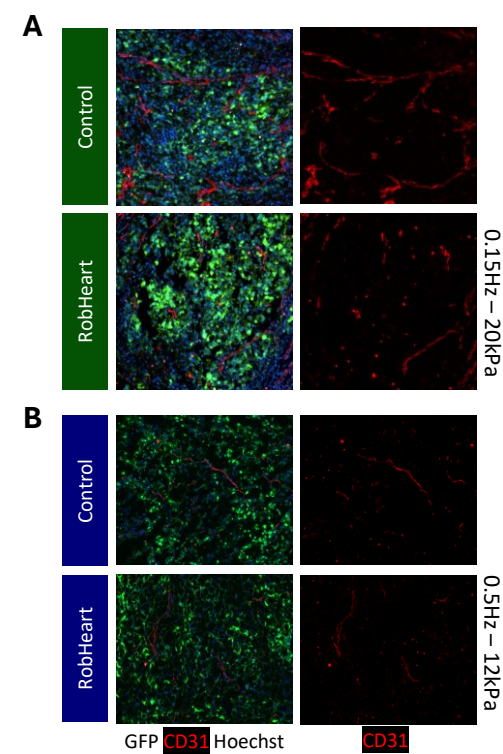


Cyclic mechanical stimulation does not promote metastatic dissemination

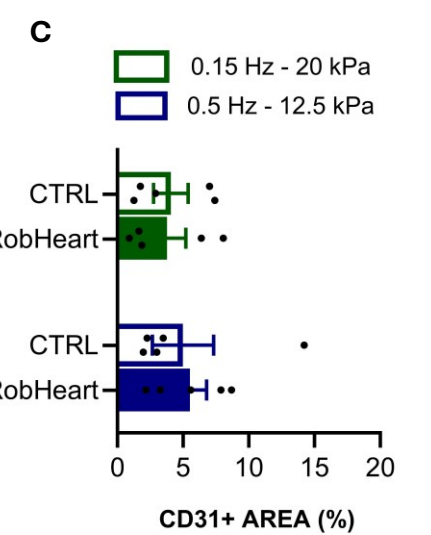


A-D. Quantification of GFP expression levels in melanoma tumors, hearts, lungs, and livers across stimulation parameters (0.15 Hz–20 kPa and 0.5 Hz–12.5 kPa).

Cyclic mechanical stimulation does not alter vessel density



A-B. Immunofluorescence of GFP+ melanoma tumor masses stained for CD31 under different mechanical stimulation conditions. C. Quantification of vascular density across stimulation parameters (0.15 Hz – 20 kPa and 0.5 Hz – 12.5 kPa).



CONCLUSIONS

- Cardiac-inspired cyclic mechanical stimulation significantly reduces melanoma tumor growth in vivo.
- Tumor suppression is associated with a decrease in cancer cell proliferation and depends on specific stimulation parameters.
- No evidence of enhanced metastatic dissemination was observed following treatment.
- Cyclic mechanical stimulation represents a promising non-invasive strategy for local tumor control and warrants further investigation as a novel cancer therapy.

REFERENCES

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