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Nanohyperthermia softens tumors to improve treatment

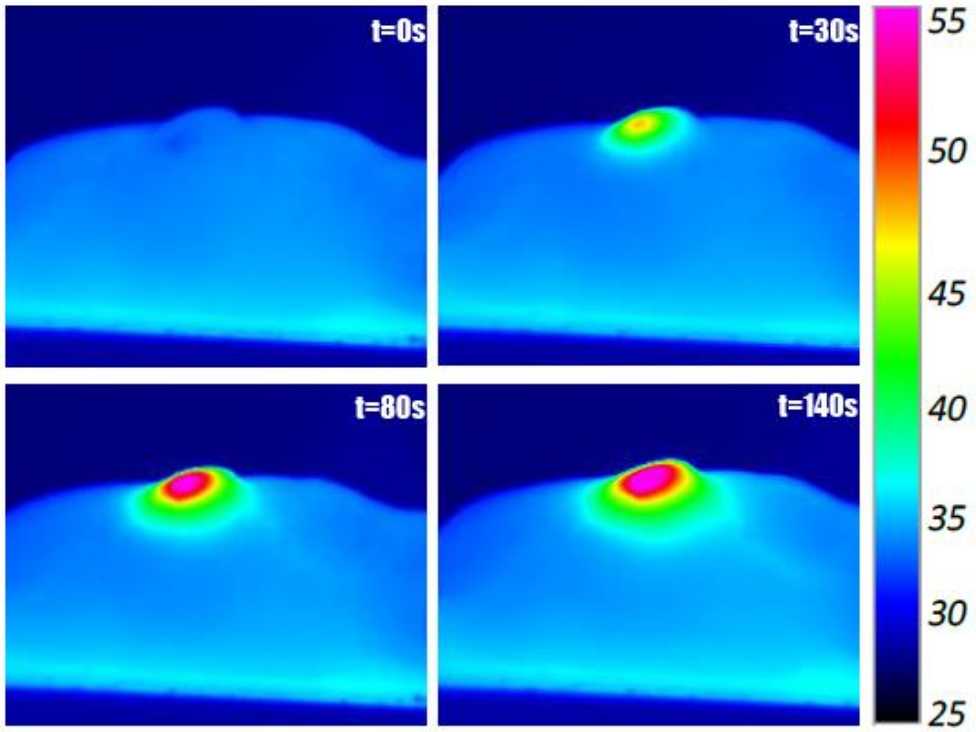
The mechanical resistance of tumors and collateral damage of standard treatments often hinder efforts to defeat cancers. However, a team of researchers from the CNRS, the French National Institute of Health and Medical Research (INSERM), Paris Descartes University, and Paris Diderot University has successfully softened malignant tumors by heating them. This method, called *nanohyperthermia*, makes the tumors more vulnerable to therapeutic agents. First, carbon nanotubes (CNTs) are directly injected into the tumors. Then, laser irradiation activates the nanotubes, while the surrounding healthy tissue remains intact. The team's work was published on January 1 in *Theranostics*.

Researchers are increasingly turning their attention to the mechanical factors affecting tumor development. Tumors stiffen due to the abnormal organization of the collagen fibers and extracellular matrix (ECM) that hold cells from the same tissue together. In addition to being a marker of malignancy, such stiffening may help cancer cells proliferate and metastasize. Furthermore, the ECM forms a physical barrier that limits tumor penetration by therapeutic agents. Various treatments attempt to disrupt the structure of tumors but are double-edged swords: as ECM is common to tumors and healthy organs, degrading it does as much harm as good.

Yet the team found a way around this problem for mouse tumors. After being directly injected into the tumors, CNTs were activated with near-infrared light. The laser only acts on areas of CNT concentration, heating them up. The researchers monitored tumor stiffness noninvasively using ultrasound shear wave elastography. This technique uses the shear or secondary wave produced by ultrasound to map tissue elasticity. In two consecutive sessions at a day's interval, the tumors were exposed to nanohyperthermia, or localized heating to 52 °C for a duration of 3 minutes. Tumors initially became more rigid before gradually softening over the 10 days or so that followed the procedure. Nanohyperthermia denatures collagen fibers locally and reduces the rigidity and volume of tumors over the long term. It disrupts the tumor microenvironment and may prove effective as an adjuvant treatment with chemotherapy.

The members of the team hail from the Laboratoire matière et systèmes complexes (CNRS, Paris Diderot University)[1], the Cochin Institute (CNRS, INSERM, Paris Descartes University), the Laboratoire d'immunopathologie et chimie thérapeutique (CNRS), and the Langevin Institute (CNRS, ESPCI Paris).

[1] *Website of the research group: http://biother.net/*



Infrared images showing laser irradiation of nanotube-injected tumor in an anaesthetized mouse. The bar on the right indicates surface temperatures (°C). © Iris Marangon

Bibliography

Tumor stiffening, a key determinant of tumor progression, is reversed by nanomaterial-induced photothermal therapy, Iris Marangon, Amanda A. K. Silva, Thomas Guilbert, Jelena Kolosnjaj-Tabi, Carmen Marchiol, Sharuja Natkhunarajah, Foucault Chamming's, Cécilia Ménard Moyon, Alberto Bianco, Jean-Luc Gennisson, Gilles Renault, Florence Gazeau. *Theranostics,* 1 January 2017.

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