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Press release

Brain tumours: for the first time, ultrasound makes blood vessels permeable to enhance treatment delivery

Teams from the Paris Public Hospitals (AP-HP), Pierre and Marie Curie University, Inserm and the CarThera company (which is hosted by the Brain and Spine Institute [ICM]), coordinated by Prof. Alexandre Carpentier, a neurosurgeon at Pitié-Salpêtrière Hospital, AP-HP, have successfully used ultrasound to temporarily permeabilise blood vessels in the brains of patients affected by recurrent malignant brain tumours. This innovative method allows increased delivery of treatments, including chemotherapeutic agents, to the brain, and represents hope for other brain pathologies. This work was published on 15 June in the international journal *Science Translational Medicine*.

Treatment of primary malignant brain tumours is currently based on a neurosurgical procedure followed by sessions of chemotherapy and/or radiotherapy. These treatments bring about disease remission for varying periods, depending on the patient. The blood-brain barrier (BBB), this particularly impermeable wall of vessels that limits the exposure of the neurons to toxic agents, restricts the entry and hence the delivery of treatments to the brain.

Given this observation, the respective teams led by Prof. Alexandre Carpentier and Dr Ahmed Idbaih, and the neuro-oncology group from Pitié-Salpêtrière Hospital, AP-HP, launched a phase 1/2a clinical trial in July 2014, sponsored by AP-HP, in patients with recurrent malignant brain tumours. The objective is to permeabilise the blood-brain barrier, in order to increase the penetration and delivery of chemotherapeutic drugs to the brain, using the "SonoCloud®" ultrasound device developed by the CarThera company. Implanted in the thickness of the skull bone, this device is activated a few minutes before intravenous injection of the product. Two minutes of sonication is enough to temporarily permeabilise the BBB for 6 hours, thereby allowing a 5-fold greater delivery of the drug to the brain than would normally happen.

To date, and for the first time in the world, several repeated "openings" of the BBB could be observed in the 20 patients treated. Moreover, tolerance is excellent: the technology invented by Prof. Carpentier and developed by the CarThera company, with the help of the Inserm LabTAU physics laboratory, does not damage the neurons, and the BBB spontaneously closes again 6 hours after the intravenous infusion.

According to Prof. Alexandre Carpentier, “this innovative method offers hope for the treatment of brain cancers, as well as other brain pathologies, such as, potentially, Alzheimer’s disease, where the existing drugs have difficulty in penetrating the brain. This technique must continue to undergo evaluation to allow its entry into routine clinical use in a few years.”

About AP-HP:

AP-HP is an internationally renowned university hospital system with a European dimension. Its 39 hospitals receive 8 million patients a year, in clinics, emergency departments, and through planned hospital admissions or home hospitalisation. It provides a public health service for all, on a 24-hour basis, which for AP-HP is a matter of both duty and pride. AP-HP is the biggest employer in Île-de-France: 95,000 people – physicians, researchers, allied medical staff, administrative staff and other employees – work there. <http://www.aphp.fr>

About CarThera:

Specialising in therapeutic ultrasound, CarThera designs and develops innovative medical devices for the treatment of brain pathologies. A spin-off company of the Paris Public Hospitals and Pierre and Marie Curie University (UPMC), CarThera is carrying out development work on the research studies and inventions of Prof. Alexandre Carpentier, a neurosurgeon at Pitié-Salpêtrière Hospital, AP-HP, internationally recognised in the area of new technologies as applied to the brain.

CarThera has developed the SonoCloud®, an intracranial ultrasound implant that makes it possible to temporarily open the blood-brain barrier (BBB). This permeabilisation of the blood vessels in the brain allows up to a seven-fold increase in the delivery of therapeutic agents to the brain, including chemotherapeutic agents, without increasing either the dose or the toxicity. A phase 1/2a clinical trial is underway for glioblastoma, a pathology for which there are very few therapeutic options. The first results, supported by a publication in the scientific journal Science Translational Medicine, confirm the therapeutic potential of SonoCloud. Penetration of the BBB, a world first, also opens possibilities for neurodegenerative indications such as Alzheimer’s disease.

Founded in 2010 by Prof. Alexandre Carpentier, CarThera is based at the Brain and Spine Institute (ICM) in Paris, and has laboratories in Lyon (Bioparc Laënnec). The company, directed by Frédéric Sottolini, collaborates closely with Inserm’s Laboratory of Therapeutic Applications of Ultrasound (LabTAU), and has been supported since its creation by the French National Research Agency (ANR), the Ministry of Research, the Île-de-France region, Bpifrance, Medicen Paris Region and Lyonbiopôle.

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