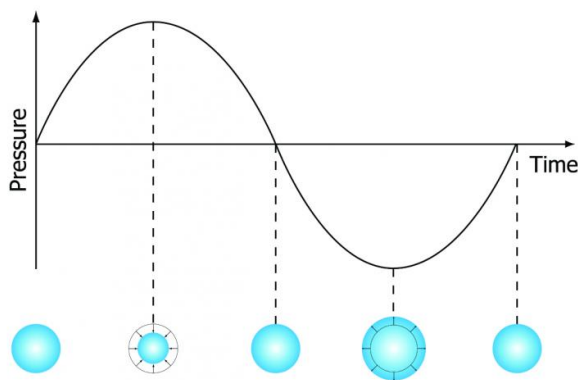


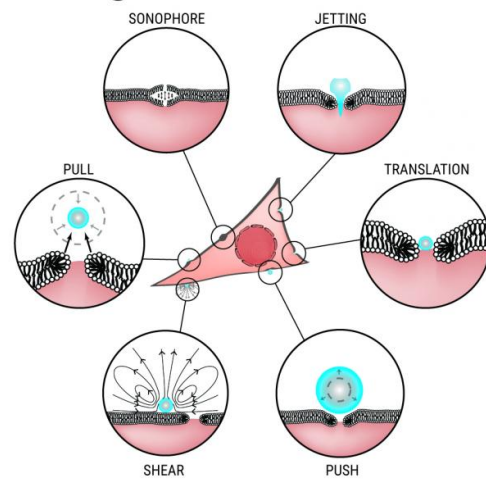
Dialing up chemotherapy for pancreatic cancer with ultrasound

May 25 2016

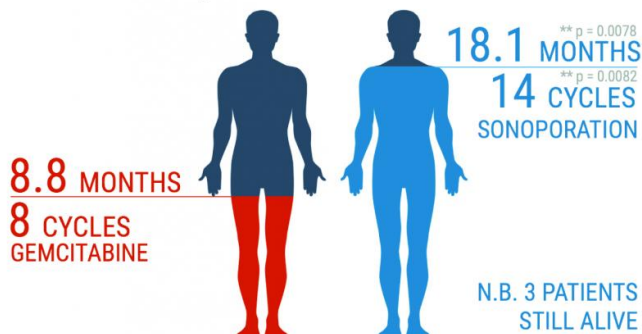
A Microbubble Oscillations



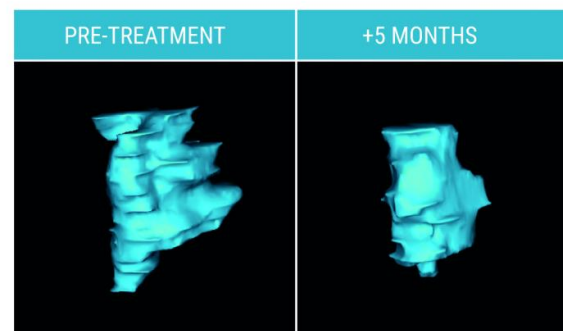
B Targeted Cell Permeation



C Improved Survival



D Tumour Regression



A microbubble (2micron in diameter) is excited by an ultrasound wave (A), which in turn interacts with a cell in many different ways allowing increased drug uptake (B). When performing this in patients, more treatment can be performed, survival increases (C) and tumour recession can be observed (D).

Credit: S. Kotopoulis/Haukeland University Hospital, Norway

Researchers at Haukeland University Hospital in Bergen, Norway have combined a laboratory ultrasound technique called "sonoporation" with the commercially-available chemotherapy compound Gemcitabine to increase the porosity of pancreatic cells with microbubbles and to help get the drug into cancer cells where it is needed.

This week at the Acoustical Society of America's 171st meeting, held May 23-27 in Salt Lake City, they are reporting some initial results, based on the outcomes of a phase I clinical trial involving 10 people undergoing treatment for pancreatic cancer. They found the new approach nearly doubled the median survival time from 7 months to 18 months without increased chemotherapy dosage and with no added toxicity or additional side effects.

"When we compared the amount of treatment our patients were able to undergo, compared to a historical cohort, we saw a significant increase of treatment cycles," said Spiros Kotopoulos, a researcher at National Centre for Ultrasound in Gastroenterology at Haukeland University Hospital in Bergen and The Departments of Clinical Science & Medicine at the University of Bergen, where some of his collaborators are also based.

Before the technique is proven effective, approved for routine care and made widely available to patients with this type of cancer, it must undergo further testing in clinical trials involving more patients—something that may take years. Nevertheless, these results are promising for a disease with an often poor prognosis. The one-year survival rate for all stages of pancreatic cancer combined is 20 percent, and the five-year survival rate is 6 percent, according to the American Cancer Society.

The concept of delivering payloads via ultrasound, sonoporation, has been around for decades, and was initially used to enhance gene uptake.

Kotopoulos became involved while working on his doctorate at the University of Hull in the United Kingdom, ultimately delving into interactions between cells and bubbles during short bursts of ultrasound exposure.

During that time, a collaboration with a group of French biologists led to the technical development of forcing single microbubbles into a cell with ultrasound—opening the door to forcing any number of other compounds into the cell. As one of the largest barriers to a drug's efficacy is its ability to permeate a cell membrane, this was a significant development—one Kotopoulos took with him to a postdoctoral fellowship in Bergen, translating the laboratory concepts to a clinical bedside.

For their phase I clinical trial, Kotopoulos and his colleagues recruited a cohort of 10 volunteers who had locally advanced or metastatic pancreatic adenocarcinoma. To facilitate more rapid clinical translation, the researchers and clinicians agreed to use technology and materials already available on the market at every step.

"If this worked, in 20 years, we didn't want a hospital to have to purchase specialized, expensive, one-use equipment," he said.

Their equipment consisted of a slightly older clinical diagnostic ultrasound scanner, the GE Logiq 9, combined with a 4C abdominal ultrasound probe. Using a diagnostic ultrasound scanner also allowed them to see and treat the tumor in real time. To generate the microbubbles, the researchers used SonoVue, a sulphur hexafluoride-based solution commonly used to help diagnose liver lesions through ultrasound. Since the bubbles are only stable in the blood stream for a few minutes, the researchers decided to inject a small amount every three and a half minutes.

For chemotherapy, the researchers used a drug called Gemcitabine.

"At the time, this was the best option for extending survival in patients with [pancreatic cancer](#)," Kotopoulos said.

The clinicians began the procedure by administering standard chemotherapy to the patients according to the existing protocol. Once the chemotherapeutic concentration in the blood reached its maximum, the researchers used the ultrasound scanner to induce sonoporation for 31.5 minutes, at 3.5 minute intervals.

According to Kotopoulos, the microbubble's permeability-enhancing mechanism of action is somewhat opaque, but is believed to be one of two methods.

At high acoustic pressures, microbubbles undergo inertial cavitation—an implosion that creates tiny pores in the cell, allowing a greater concentration of drugs to enter. This effect, which includes shockwaves, may penetrate deeper into the tissue, thus having a deeper effect. Due to potentially violent ripple effects—similar to throwing a cannonball against a wall—this is generally avoided, Kotopoulos said.

At low to moderate acoustic pressures, the bubbles tend to interact with cells, bouncing and rolling against them to push and pull the membrane, occasionally entering the cells—more akin to cracking open a safe by drilling some small, precise holes.

When treated with sonoporation, the volunteers were able to undergo 14 (± 6) cycles of treatment, versus 8 (± 6) with normal chemotherapy.

This ultimately had the effect of stabilizing or decreasing the tumor volumes in 50 percent of the patients and increasing the median patient survival time from approximately 7 months to 18 months.

Future work for Kotopoulos and his colleagues will include performing a larger-scale phase I/II clinical trial with international collaborators, and working to develop a microbubble compound optimized for targeted drug-delivery at low acoustic intensities. They will also seek to fully understand the mechanisms of sonoporation by using advanced mouse models and bioreactors.

More information: Presentation #3aBA6, "Ultrasound- and microbubble-enhanced chemotherapy for treating pancreatic cancer: A phase I clinical trial," by Spiros Kotopoulos will take place on Wednesday, May 25, 2016, at 10:10 a.m. MDT in Salon H. The abstract can be found by searching for the presentation number here: acousticalsociety.org/content/...ng-itinerary-planner

Provided by Acoustical Society of America

Citation: Dialing up chemotherapy for pancreatic cancer with ultrasound (2016, May 25) retrieved 17 May 2024 from <https://medicalxpress.com/news/2016-05-dialing-chemotherapy-pancreatic-cancer-ultrasound.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--