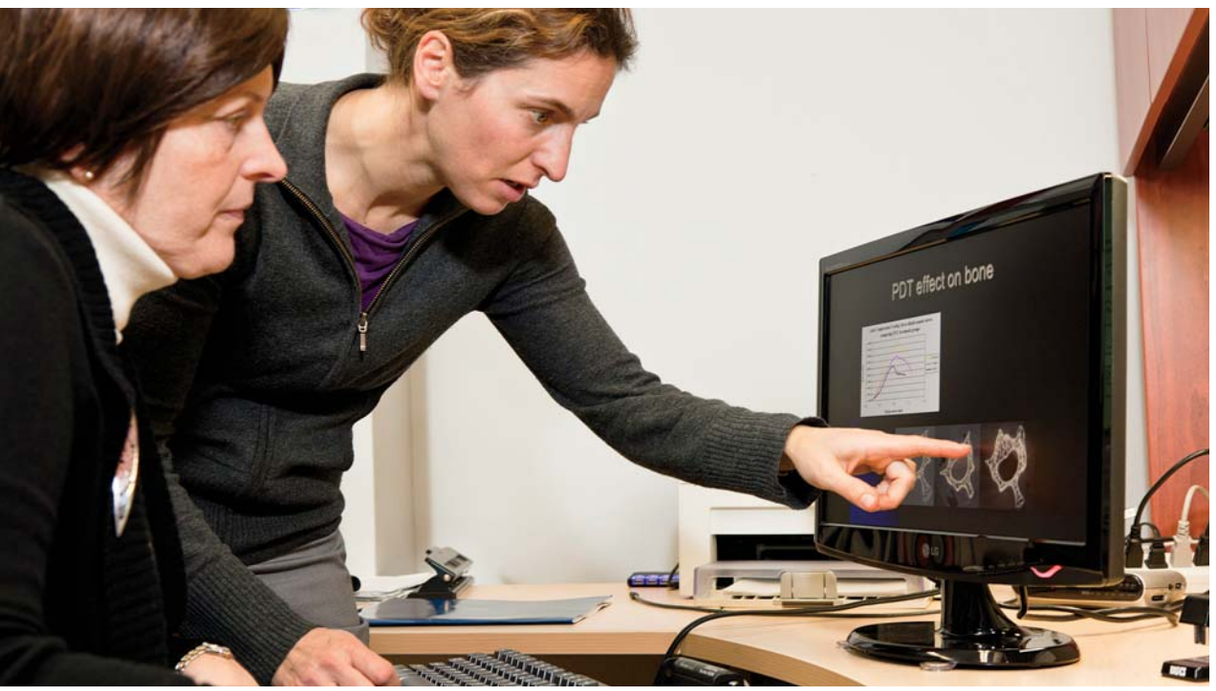
# A BRILLIANT COMBINATION

Musculoskeletal researchers are pairing light and drugs to effect a more powerful way to kill cancer that has migrated to bone




DRS. MARGARETE AKENS AND CARI WHYNE

Imagine that your body could be healed by light.

That's what scientists at Sunnybrook Research Institute (SRI) are investigating using therapeutic photosensitizers—light-sensitive drugs—to treat patients with cancer that has spread to their spine.

Photodynamic therapy, also known as PDT, is a minimally invasive, safe and effective procedure that has been used around the world since the 1980s. It has been used to treat cancer of the skin, brain, breast and lung, and other diseases (for example, age-related macular degeneration, a disease of the eye that can lead to vision loss).

Photodynamic therapy combines a light-sensitive drug that selectively accumulates in cancer cells with locally applied light at a specific wavelength delivered via a laser. Together, the photosensitizer and light produce a reactive form of oxygen that destroys the cancer cells and shrinks the tumour.

About 75% of women with metastatic breast cancer have metastases in the bone, most commonly in the spine. This can lead to severe pain, fracture, structural instability of the spine and even spinal cord injury resulting in paralysis. A PDT approach adds to and complements available treatments such as bisphosphonates (drugs used to treat bone loss and prevent fractures) and radiation therapy, which are not effective in all patients.

In 2010, Drs. Margarete Akens, Cari Whyne and Albert Yee from the Holland Musculoskeletal Research Program at SRI, and colleagues published the results of a preclinical study on the use of PDT for spinal metastases in the journal *Breast Cancer Research and Treatment*.

The study examined which drug and light dose would best destroy tumours within the spine while protecting sensitive tissues nearby, such as the spinal cord and nerve roots.

Akens, a junior scientist in the labs of Yee and Whyne, conducted the study on a preclinical model using human breast cancer cells. After the presence of tumour cells within the spine was confirmed with bioluminescence imaging (labelling the cancer cells so that they will emit light), Akens performed PDT using different concentrations of a light-sensitive drug and altering how long a wavelength-specific light was delivered to the tumours. The best combination of drug and light dose resulted in cancer cell death and smaller tumours 80% of the time, while protecting the critical elements surrounding the spine.

"I was impressed to see the tumours destroyed and to have such a significant success rate each time I repeated the experiment," says Akens.

"In addition to killing tumour cells, we needed to protect and preserve the neural elements of the spine. We also needed to optimize our understanding of how PDT affects the bony elements of spine," says Yee, who is also a staff spine surgeon and orthopaedic coordinator for the bone metastasis clinic at Sunnybrook's Odette Cancer Centre, and co-director of the University of Toronto's department of surgery spine program.

While there is research and clinical evidence suggesting that PDT is an effective cancer therapy, little is known about how PDT affects bones.

In 2010, Akens, Whyne, Yee and collaborators published another study, this

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Dr. Albert Yee

one in the journal *Spine*, "Effects of Photodynamic Therapy on the Structural Integrity of Vertebral Bone."

In the lab of Whyne, who is the director of the Holland Musculoskeletal Research Program at SRI and an associate professor in surgery at U of T, the triad conducted biomechanical testing and structural image analysis on healthy rats to see how bone would react when treated with PDT.

"We were very surprised to see that the bone became stronger, and that there was significant improvement in bone formation and mechanical stability after the treatment," says Akens.

In yet another study published the same year, the researchers observed that there might be an additive or synergistic effect to bony stability when PDT is combined with bisphosphonates. This is important because many cancer patients with bony metastasis are routinely treated with bisphosphonates.

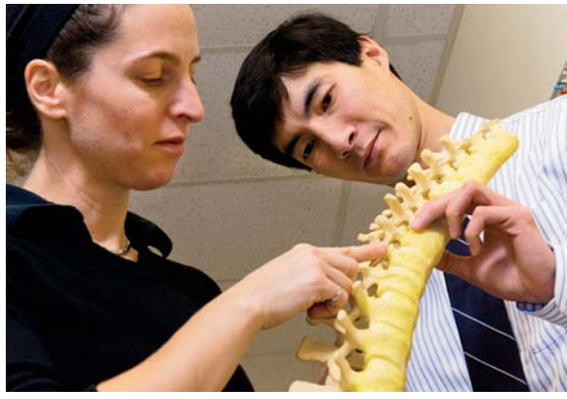
As a result of the researchers' successful preclinical work, the team has received funding for a phase 1 clinical trial to evaluate the safety of PDT for the treatment of spinal metastases. Yee says he expects the trial to begin early in 2011 with patients at Sunnybrook.

Researchers will give the light-sensitive drug intravenously. They will insert an optical laser fibre via a needle into the tumour within the spine, and turn on the light to destroy the tumour and potentially strengthen the remaining bone. This will be performed as an adjunct procedure for patients who are receiving vertebroplasty therapy to strengthen their diseased bony spine.

As the team prepares for the clinical trial, they say they are confident that PDT has the potential to change the way patients with cancer that has spread to the spine are treated. "It's a way to kill tumour cells locally and improve the stability biologically of the surrounding bone," says Whyne.

—Eleni Kanavas

Supporting this research are the Canadian Breast Cancer Foundation, Ontario chapter; Canadian Breast Cancer Research Alliance; Canadian Institutes of Health Research and Ontario Institute for Cancer Research. The Canada Foundation for Innovation and Ontario Ministry of Research and Innovation provided infrastructure support.



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