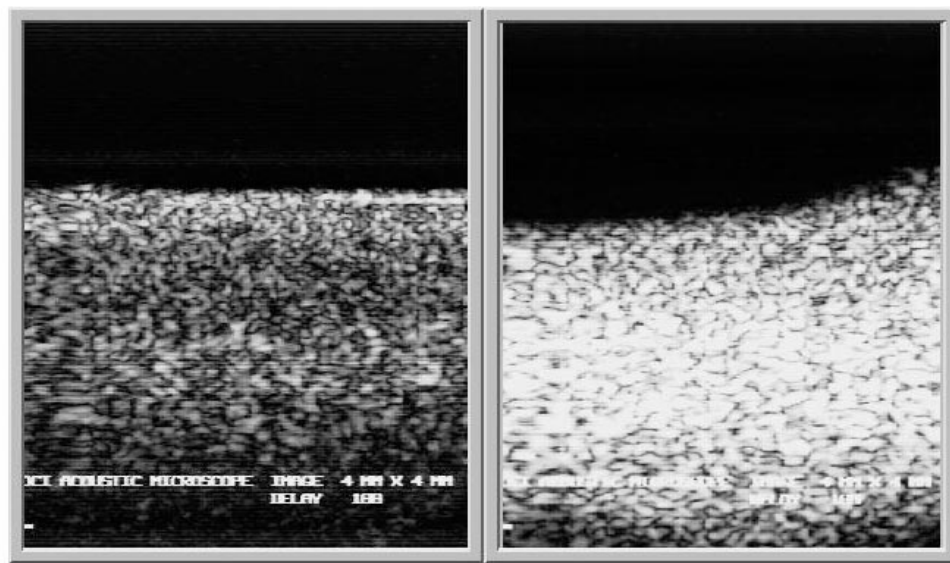


## Ultrasound Biomicroscopy: A Promising Candidate for Monitoring Tumour Response to Therapy in Cancer Patients

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(a) Untreated control pellet

(b) 24 hours after treatment with cisplatin, a drug commonly used in chemotherapy that causes apoptosis.

FIGURE 1. Ultrasonic images of AML-5 cell pellets (4 mm in each panel). The changes in ultrasonic speckle intensity are associated with the cell of apoptosis.

In patients with cancer, tumour responses to therapy are typically measured three to four weeks into the course of treatment. A combination of inspection, palpation, biopsy, and radiographic imaging of the tumour is currently used to determine whether treatment has been successful. However, these methods have shortcomings; an ideal procedure would be non-invasive, accurate, and one that could be performed shortly after the initiation of therapy. These criteria may soon be met with the introduction of high frequency ultrasound biomicroscopy (UBM) in the clinical setting.

UBM was first developed by Dr. Michael Sherar in the late 1980's at the Ontario Cancer Institute/Princess Margaret Hospital in Toronto with then Ph.D. supervisor Dr. Stuart Foster. Its imaging potential was demonstrated in the differentiation of necrotic and viable cells in tumour spheroids.<sup>1</sup> Since then, the applications of UBM have expanded rapidly to include the diagnosis and assessment of ocular disease,<sup>2</sup> currently performed at many centers including the Eye Clinic at Princess Margaret Hospital, and of psoriasis.<sup>3</sup> It has also been used to study embryonic brain development in mice.<sup>4</sup>

The idea of employing UBM in cancer care centers is a recent one, and is being investigated by a team of researchers at Princess Margaret Hospital including Drs. Gregory Czarnota, Michael Kolios, Michael Sherar, and John Hunt. Current cancer treatment, including radiation therapy and chemotherapy, works by inducing apoptosis in tumour cells, a process to which UBM is exquisitely sensitive. Nuclear condensation and fragmentation, changes that characterize apoptosis, lead to a six-fold increase in the amount of ultrasound backscatter.<sup>5</sup> Consequently, areas of tissue with apoptotic cells appear very bright in a conventional ultrasound B-scan image as compared to viable cells (Figure 1). Preliminary data from studies involving patients with superficial lymphoma and melanoma demonstrate a large increase in ultrasound scattering after the onset of therapy as compared to pre-treatment.

As a clinical tool to assess tumour response to therapy, UBM provides several advantages over current practices. The non-invasive nature of the procedure results in minimal discomfort to the patient and, hence, allows for more frequent monitoring. Moreover, UBM provides a means of detecting apoptosis over the entire volume of tumour and surrounding tissues. Most importantly, the expediency at which apoptosis can be detected by UBM allows for the timely detection of resistant tumours and for timely treatment modifications.

However, the very fine resolution and high contrast enjoyed by UBM comes at a price: lack of penetration depth. Imaging with ultrasound in the 40-100 MHz range is limited to a depth of approximately 3-5 mm, depending on the tissue type.

Consequently, UBM has been restricted to imaging superficial tissues, such as the skin and the anterior chamber of the eye. This may soon be overcome with the development of needle and catheter-based UBM systems for imaging deeper tissues and blood vessels *in situ*.

Many questions surrounding the use of UBM still persist and require active investigation. Nevertheless, the foundations have been laid and the outlook is promising. In time, UBM may become part of a standard and comprehensive treatment plan for patients with cancer.

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