

## The promise and challenge of minimally invasive therapy

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Minimally invasive therapy for localized prostate cancer provides an alternative treatment option for men who decline surveillance and who opt against standard radical prostatectomy or external beam radiotherapy.

These therapies include brachytherapy, photodynamic therapy, interstitial microwave thermal ablation, high-intensity focused ultrasonography and cryotherapy. Each modality ablates tissue through the guided application of energy to an area of interest that usually includes the whole prostate, with the exception of cryotherapy, which employs ultracold rather than radiant energy for the task.

The perceived benefits of minimally invasive therapy include the convenience of a less invasive treatment that can be completed in 1 or a few sessions, and a belief that the more precise control of treatment delivery will result in an improved toxicity profile compared with conventional therapies.

For investigators, these modalities also hold promise as a salvage treatment for local failures of external beam radiotherapy, or as a focal treatment of a dominant prostate lesion, and these uses are presently under investigation. The efficacy of focal prostate therapy to cure prostate cancer will rely on the ability of modern imaging technologies such as functional magnetic resonance imaging to accurately identify the dominant lesion in the prostate, and this ability remains to be determined in clinical trials.

The advantages of enhanced precision and control in the delivery of minimally invasive therapies are also paradoxically their weaknesses. These modalities are very unforgiving, and any treatment that offers millimetre precision in delivery also means that a misplacement of even a few millimetres of applied therapy may result in undertreatment of the tumour or overtreatment of a critical healthy structure, and an unacceptable outcome.

The optimal application of a minimally invasive therapy first requires an understanding of the dose-response characteristics of the tumour and critical healthy tissues for the modality employed. Second, it requires an ability to accurately model the treatment in advance (preplan) to best cover the tumour and protect healthy tissues. Finally, it requires the technology and operator skill to precisely recreate this plan in real time, in the patient. It is apparent that all these modalities are both operator-dependent and very much technology-driven. Advances in planning, imaging, treatment

delivery and clinical experience have improved tumour and toxicity outcomes, particularly for brachytherapy and cryotherapy, which have the longest history and are the most extensively investigated.

Similarly, appropriate patient selection is critical for a favourable outcome, since none of these modalities can safely and reliably treat very far beyond the prostate capsule, and they are all best limited to the treatment of patients with low-risk disease.

The paper by Chalasani and colleagues<sup>1</sup> in this edition of *CUAJ* brings our attention to cryotherapy, which, as the authors state, has a very long history somewhat marred by severe toxicity in the early experience. However, better patient selection, newer technology and the application of the principles outlined above have improved outcomes in more recent reports.<sup>2</sup>

The authors do not provide any clinical data, but rather a description of a third-generation ultrasonography unit that provides real-time 3-dimensional visualization of the procedure. They predict that this will lead to improved precision and better outcomes, although this needs confirmation in clinical trials.

Prostate brachytherapy remains the gold standard for minimally invasive therapy because the toxicity profile and tumour outcomes for appropriately selected patients are predictable and favourable, having been well documented in large-scale prospective trials. Cryotherapy and the other minimally invasive modalities hold promise but all must be rigorously scrutinized in large-scale prospective trials before being accepted as standard therapy.

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