

## Focal Therapy Will Become a Standard Option for Selected Men With Localized Prostate Cancer

**TO THE EDITOR:** Giannarini et al<sup>1</sup> provide a fairly vigorous case to preserve the status quo for men diagnosed with localized prostate cancer that are contemplating therapy. We saw similar pleas by the mastectomy proponents when radical mastectomy was being challenged by lumpectomy.<sup>2</sup> More recently, similar arguments were made when partial nephrectomy was being proposed as a more suitable alternative for many.<sup>3</sup> It is interesting to reflect, despite the early protestations, which approach (whole organ *v* tissue preserving) is now considered the practice standard for the majority of eligible patients; in the case of renal cancer without level 1 evidence. Prostate cancer is the last solid organ cancer in which therapy is directed to the total extent of the tissue. The key revolutions in breast and kidney care came about through developments in imaging (mammography and computed tomography scanning, respectively) that accurately localized the tumor. In prostate cancer, we have relied on a diagnostic strategy that cannot accurately localize tumors; the decision to remove or irradiate a prostate has been a binary one based on the presence or absence of cancer.

We, and others, believe that the era of accurately depicting location in prostate cancer has arrived and with such a paradigm shift the opportunity of exploiting tumor location<sup>4</sup> provides an avenue to selective therapy that can confer benefit to both patients and health care systems.

There are a number of reasons why a tissue-preserving approach should be entertained:

First, there is little to lose. If maximal therapy (radical prostatectomy) failed to confer any significant survival benefits over observation in the latest study,<sup>5</sup> it is unlikely that we are going to see any differences in survival between two types of therapy—whole gland and tissue preserving.

Second, we need to do something different. Changing our means of access through expensive capital investments into robotic-assisted surgery but doing the same operation has not improved outcomes but has certainly increased costs.<sup>6</sup>

Third, there is plenty of tissue to be preserved. The mean cancer volume at diagnosis varies between 1-2 cm<sup>3</sup> depending on the intensity of screening.<sup>7</sup> Most prostates are around 40 cm<sup>3</sup> in volume. Even with the application of a margin it should be possible to preserve well over half the prostate in the majority of eligible patients.

Fourth, preserving prostate matters. Two registered, prospective trials have shown that the majority of men (95%) treated in a tissue-preserving manner are indistinguishable from their status before the intervention.<sup>8</sup> This compares with 20% men preserving erectile function and 80% urinary continence 2 years after radical treatment when similar instruments were used in a formal trial setting to elicit functional status.<sup>5</sup>

Fifth, the diagnostic pathway is changing. In many centers around the world the response to an elevated prostate-specific antigen level is not a biopsy, but imaging in the form of multiparametric magnetic resonance imaging to derive location. The information on location will be used to inform a targeted biopsy.<sup>4</sup> If the entire prostate need not be sampled men will ask why their entire prostate needs to be subjected to therapy.

Sixth, our understanding of disease is changing. There is growing evidence that Gleason pattern 3 represents a phenotype that is incapable of metastatic spread.<sup>9</sup> We and others have suggested that it should be redesignated as a noncancer.<sup>10</sup> It follows that most secondary lesions within the prostate—and they do exist as most men have two to three cancers at diagnosis—are of no malignant potential. Therefore, the worry of leaving cancer behind echoes the pleas of the mastectomists that have, with time, proven to be spurious.

Finally, Giannarini et al<sup>1</sup> state no conflicts of interest. We, as surgeons, are all conflicted. To dedicate oneself to a technique through arduous training makes it hard to give up. Most of us make a living from these procedures and gain professional esteem from our activity through grants, publications, and lectures. What we do need to do is to listen to patients and the utilities they place on preserving genitourinary function and also in what they require in terms of cancer-related risk reduction. There is strong evidence that we are not serving their needs particularly well at present.<sup>5</sup> A rapid, but critical phased development program of this new technology is what is required in which we pool resources to create as many opportunities for patients to get into as many trials or registries as possible.<sup>8</sup>

Things can and do change quickly. Breast surgeons performing mastectomy, urologists performing nephrectomy, and vascular surgeons performing open aneurysm repairs have all changed. Not changing in our management of prostate cancer is not an option.

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### AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at [www.jco.org](http://www.jco.org).

## REFERENCES

1. Giannarini G, Gandaglia G, Montorsi F, et al: Will focal therapy remain only an attractive illusion for the primary treatment of prostate cancer? *J Clin Oncol* 32:1299-1301, 2014
2. Fisher B: The revolution in breast cancer surgery: Science or anecdotalism? *World J Surg* 9:655-666, 1985
3. Touijer K, Jacqmin D, Kavoussi LR, et al: The expanding role of partial nephrectomy: A critical analysis of indications, results, and complications. *Eur Urol* 57:214-222, 2010
4. Moore CM, Robertson NL, Arsanious N, et al: Image-guided prostate biopsy using magnetic resonance imaging-derived targets: A systematic review. *Eur Urol* 63:125-140, 2013
5. Wilt TJ, Brawer MK, Jones KM, et al: Radical prostatectomy versus observation for localized prostate cancer. *N Engl J Med* 367:203-213, 2012
6. Gandaglia G, Sammon JD, Chang SL, et al: Comparative effectiveness of robot-assisted and open radical prostatectomy in the postdissemination era. *J Clin Oncol* 32:1419-1426, 2014
7. Wolters T, Roobol MJ, van Leeuwen PJ, et al: A critical analysis of the tumor volume threshold for clinically insignificant prostate cancer using a data set of a randomized screening trial. *J Urol* 185:121-125, 2011
8. Valerio M, Ahmed HU, Emberton M, et al: The role of focal therapy in the management of localised prostate cancer: A systematic review. *Eur Urol* 2013 doi: 10.1016/j.eururo.2013.05.048. [Epub ahead of print]
9. Ross HM, Kryvenko ON, Cowan JE, et al: Do adenocarcinomas of the prostate with Gleason score (GS)  $\leq$  6 have the potential to metastasize to lymph nodes? *Am J Surg Pathol* 36:1346-1352, 2012
10. Ahmed HU, Arya M, Freeman A, et al: Do low-grade and low-volume prostate cancers bear the hallmarks of malignancy? *Lancet Oncol* 13:e509-e517, 2012

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