

# Recent advances in focal therapy of prostate and kidney cancer

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## Abstract

The concept of focal therapy in oncologic surgery refers to maximizing healthy tissue preservation while maintaining excellent cancer control outcomes. Herein, we address the recent advantages in the field of focal therapy for both kidney and prostate cancer, focusing on technological achievements and future perspectives.

## Introduction and context

The concept of focal therapy in oncologic surgery refers to maximizing healthy tissue preservation while maintaining excellent cancer control outcomes by targeting and destroying only the cancer. Preserving healthy non-malignant prostate tissue while treating known areas of prostate cancer (PCa) may translate into quality-of-life benefits such as potency and continence [1]. On the other hand, nephron-sparing surgery (NSS) in kidney cancer treatment preserves renal function and reduces the chance of end-stage renal disease.

NSS is a widely accepted option in the treatment of renal masses, in which partial nephrectomy represents the standard of care for localized renal masses. However, the concept of focal therapy for PCa has been debated and will remain under development before it can be widely introduced into routine clinical practice. Herein, we address recent advances in the field of focal therapy for both kidney cancer and PCa, focusing on technological achievements and future perspectives.

## Recent advances

### **Focal therapy of prostate cancer**

From the standpoint of the clinician, there are three questions that need clarification before considering focal therapy as routine. First, who are the appropriate candidates for focal therapy? Second, what are the treatment options and what is their efficacy for targeting

and destroying prostate tissue? Finally, what are the outcomes and how should patients be followed?

Recent advancements on this topic regard mainly the first two questions. To be able to focally ablate cancerous tissue, we need to visualize and map the location and the extent of the disease. Currently, routine imaging techniques (ultrasound, computed tomography, magnetic resonance imaging, and radionuclear imaging) are not reliable enough to define the spatial distribution of PCa within the prostate gland. Novel imaging approaches that need validation and further investigation in a focal therapy setting include several techniques. HistoScanning™ (Advanced Medical Diagnostics, Waterloo, Belgium) is based on mathematical elaboration of raw ultrasonographic data and is used to attempt to define and characterize PCa within the gland. This technology may be promising in accurately detecting PCa foci of at least 0.5 mL, but available results are still limited [2,3] and further study is required. Contrast-enhanced ultrasound using microbubbles as contrast agents represents yet another potentially attractive option to visualize and characterize PCa [4]. Magnetic resonance technology is undergoing significant developments as well, focusing on a focal therapy application [5].

Despite extensive efforts to develop an adequate imaging technique to visualize and characterize PCa, these technologies do not represent routine clinical practice,

although their potential is evident. To date, candidate selection for focal therapy of PCa has relied largely on prostate biopsy [6], but routine office-based biopsy schemes have been shown to be unreliable for identifying appropriate candidates for focal therapy [7,8]. The trend is to accept three-dimensional, multicore, transperineal mapping biopsy as a selection tool [9] that is able to localize and define the extent of cancerous tissue while providing guidance for subsequent targeted ablation. The downside of such an extensive biopsy technique is that it requires hospitalization and is performed in the operating room under anesthesia. A roughly 10% incidence of urinary retention has been reported with the transperineal approach [10].

New technological developments for ablation are being investigated. Cryoablation and high-intensity focused ultrasound (HIFU) are well-known thermoablative technologies for focal therapy and have been studied in the clinical setting [1,11-13]. Recently, new approaches to tissue ablation have been proposed; these include laser photothermal therapy, with the recent publication of a phase I trial [14], and irreversible electroporation (which works by disrupting cell membranes with the application of impulses of electric current) using the NanoKnife™ (AngioDynamics, Queensbury, NY, USA) technology [15,16]. These approaches are in the early phases of development, but preliminary data are intriguing.

The interest in focal therapy by patients, physicians, as well as industry is growing rapidly and is accompanied by considerable research efforts both on the basic science and clinical sides. We are likely to witness even greater interest in and implementation of focal therapy for PCa in the future.

#### **Focal therapy of kidney cancer**

Due to the widespread use of abdominal imaging and the subsequent increase in the detection of incidental renal lesions without significant decline in kidney cancer mortality over the years [17], it has become evident that we now have a new clinical entity – the small renal mass (SRM). Most SRMs are amenable to NSS, which represents the gold standard for the treatment of these lesions. Minimally invasive NSS is technically challenging, thus limiting its diffusion into urological practice. In recent years, ablative technologies [cryoablation, HIFU, radiofrequency ablation (RFA), and others] have been introduced as treatment options for SRMs [18]. Currently, ablative techniques are considered alternatives to conventional surgery mass by the American Urological Association for clinical stage T1 renal mass [19].

Renal cryoablation and RFA are the most studied ablative approaches to date. These procedures can be performed both laparoscopically and percutaneously with good outcomes and limited complications. A recent meta-analysis of cryoablation and RFA results has shown good oncologic efficacy in the short term and suggested that cryoablation may be slightly superior to RFA in local tumor control and risk of disease progression [20]. From other studies, it appears that the percutaneous approach may be associated with inferior oncologic outcomes compared with the laparoscopic technique using RFA and cryoablation [21]. However, another meta-analysis found the percutaneous approach to be safer compared with the laparoscopic one in terms of complications while offering comparable oncologic outcomes [22]. Both of these retrospective meta-analyses of published series may have inclusion biases that skewed the results toward one or the other approach and are limited by their retrospective nature. While there may be no solid consensus on the superiority of one or the other technique or approach, it seems clear that these technologies offer overall good outcomes and are less technically challenging compared with laparoscopic/robotic partial nephrectomy. Therefore, ablative techniques may propagate the diffusion of focal therapy for SRMs and its advantages to more patients.

New technologies are currently being investigated for the ablation of renal masses. These include HIFU [23], irreversible electroporation [24], and microwave ablation [25]. These are in the early stages of investigation, and few preclinical, and almost no clinical, data are available. Further studies will demonstrate whether these technologies have an advantage over the current thermoablative techniques (cryoablation and RFA).

#### **Implications for clinical practice**

Focal therapy of kidney cancer is a viable approach to SMRs and is rapidly gaining popularity due to short- and mid-term oncologic efficacy and technical ease as more and more centers introduce ablative approaches into their armamentarium. Long-term oncologic outcomes are not yet available and will need to be critically assessed.

The introduction of focal therapy for PCa has a valid, albeit debatable, rationale [26]; technological advances allow for its clinical implementation, and research efforts are conspicuous in this field. These factors instill a belief that focal therapy for PCa will shortly become a clinical reality, challenging the paradigm of whole-gland therapy of PCa. The diffusion of focal therapy evidently needs well-designed trials that would provide hard scientific evidence of the advantages and the drawbacks of this innovative concept.

## Abbreviations

HIFU, high-intensity focused ultrasound; NSS, nephron-sparing surgery; PCa, prostate cancer; RFA, radiofrequency ablation; SRM, small renal mass.

## Competing interests

The authors declare that they have no competing interests.

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