

Irreversible Electroporation (IRE) for Prostate Cancer, the Present Day Status

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Irreversible Electroporation (IRE) has been used for prostate cancer since 2011. There have been clinical trials as well as anecdotal approaches [1]. Trials require a long time and need to compare many treatment types. Randomized multi-center approaches are needed. The outcome collected up to now showed hopeful results. Prospective clinical trials are required. IRE for prostate cancer should attain the stage of being recommended by international guidelines. The IRE machine (The NanoKnife) is based on direct current generator and needle electrodes [2,3]. With TRUS guidance, the electrodes are placed perineally. The probes should be placed away from the urethra, the rectum, and the sphincter to avoid damage. General anesthesia in supine position is the regime. The procedure takes about 45-90 min. A catheter is inserted for 24 hours.

Irreversible electroporation uses high-voltage electric pulses that cause cell death. These pulses travel between two or more electrodes, causing a leak in the cell membrane, formed by the creation of nanopores. Depending on the field amplitude, duration and number of electrical pulses, this process can be temporary (reversible electroporation) or permanent IRE. In the case of permanent, due to changes to the membrane, the cell will become incapable of holding on to its homeostasis and will apoptose.

Ting et al. evaluated functional and oncological outcomes in 25 patients following IRE. No significant changes in urinary, sexual or bowel function were noted (using AUA scores). At follow-up 5 patients (21%) had suspicious lesions on mpMRI, of which four (19%) proved to be significant on biopsy. All patients were leak-free continent and erectile function was reported to be stable. Valerio et al. reported on 34 patients undergoing IRE for organ-confined prostate cancer (ranging from low- to high risk disease). After a median follow-up of 6 months for 24 patients 100% of patients were continent and potency was preserved in 95% (19/20) men. Van den Bos et al. prospectively reported on 63 patients who received IRE with a minimum follow-up of 6 months. The results demonstrated no change in quality of life or mental, physical, bowel or urinary functions. A slight decrease in sexual quality of life was observed [4].

Thermal ablation methods have limitations due to the vessel heat sink effect. This protects cancer nearby vessels resulting in high recurrence rates. Quite the opposite, pathology demonstrated that IRE lesions, showed complete destruction of tissue up to the vessel wall without vessel destruction. This in the prostate, preserves blood flow to maintain potency [5].

Results from one of the largest IRE studies was recently published by van den Bos et al in which 63 patients with Gleason 6-7 disease were treated with IRE. Sixteen percent of patients had an in-treatment field recurrence and 24% were found to have persistent cancer anywhere within the prostate. No high-grade adverse events occurred and physical, mental, bowel, and urinary quality of life measures remained unchanged at 6 months postoperatively. Despite the theoretical claim that IRE might be less damaging to nerve tissue, mild declines in sexual quality of life median score from 66 to 54 at 6 months ($P < 0.001$) were seen. This novel method has yet to be investigated further in larger scaled studies [6].

Guenther et al presented 471 tissue ablation procedures in 429 patients with PCa using IRE (NanoKnife, AngioDynamics Inc., USA). Seventy patients had had PCa related treatments prior to IRE: Sixteen patients had undergone Radical Prostatectomy (RPE), twenty-three had had Radiation Therapy (RT), 5 had had both. Seventeen patients had undergone a Transurethral Resection Of The Prostate (TURP), 8 had been treated with High-Intensity Focused Ultrasound (HIFU), two of which had had the procedure performed twice. The majority ($N = 29$) of those with previous treatments had undergone Androgen Deprivation Therapy (ADT). The retrospective study concludes that Irreversible Electroporation (IRE) is a safe, effective and suitable modality for the treatment of PCa at all clinical stages and recurrent disease. Continence was preserved in all cases. The comparison of IRE with Radical Prostatectomy (RPE) revealed similar recurrence rates over time, indicating similar effectiveness of IRE to RPE. Thus the data illustrates the feasibility of IRE for PCa treatments. However, data needs to be confirmed by more systematic studies [7].

Federico Colletini reported after a median follow-up of 20 months, focal irreversible electroporation of localized prostate cancer was associated, with low urogenital toxicity and promising oncologic outcomes [8].

Since Shoulong Dong described the first trial conducted in humans involving administration of High Frequency bipolar pulses therapy for prostate cancer, it was clear that bipolar pulse is a minimally invasive nonthermal therapy in tumor ablation that can reduce the dose of muscle relaxant during treatment. Compared to radical prostatectomy and thermal therapy, it can preserve the neurovascular bundle, urethra, and major vasculature in the prostate, which is beneficial to patient recovery. The postoperative effect of such a treatment on patients was very encouraging, that is, sexual function was preserved in 14 (100%) of 14 patients, 40 (100%) of 40 patients could control urination and did not require urinal pads, and 0 of 40 patients had urinary incontinence during surgery. The clinical trials were conducted successfully, and they provided valuable insights regarding the treatment of prostate cancer using high frequency bipolar pulses, which will promote the ablation of solid tumors by IRE [9]. The clinical results collected so far has shown encouraging results and uniformly state IRE as a safe and effective treatment (at least for focal ablation) but all merit further studies.

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