



Geometric Anatomy Basis for Safe and Effective Focal Ablation of Prostate Cancer by Irreversible Electroporation (IRE)

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Abstract: Irreversible electroporation (IRE) is a recent and minimally invasive method of partial prostate ablation. However, knowledge of the essential landmarks of prostate anatomy is crucial to achieving safe and effective partial ablation by IRE. High-quality imaging of the prostate is essential before the procedure. The individual morphological pattern of the prostate must be taken into account and detailed mapping with measurement of the lesion is necessary to determine optimal needle placement. The entire tumour volume must be covered while ensuring the safety of critical anatomical structures such as the rectum, urethra, nerve bundles and sphincter muscle.

Keywords: prostate; anatomy; magnetic resonance imaging; focal ablation; irreversible electroporation



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1. Introduction

Prostate cancer (PCa) is a prevalent disease among men over the age of 50. According to the International Agency for Research on Cancer [1], the age-standardised incidence rate of prostate cancer in Europe is estimated to be around 100 cases per 100,000 men per year. The primary treatment options for localised prostate tumours are brachytherapy, radical prostatectomy and radiotherapy. However, a significant number of prostate cancers pose a low risk of progression over a 15-year period, making aggressive therapies unnecessary [2,3]. These treatments can result in a diminished quality of life without providing substantial benefits in terms of increased survival rates. Consequently, alternative approaches such as focal prostate ablation have emerged to minimise the impact on patients' quality of life. One such procedure is irreversible electroporation (IRE), which offers a recent and minimally invasive method for partial prostate ablation [4]. In this article, our aim is to provide an overview of the essential landmarks of prostate anatomy that are crucial for performing safe and effective partial ablation using IRE.

2. How IRE Works

Irreversible Electroporation (IRE) is an alternative to thermal or cryo-ablation for focal therapy of localised prostate cancer [3]. IRE effects are non-thermal and determined by a high-amplitude electric field with usually 90 pulses of 1500 volts/cm delivered between pair of electrodes [5–7] Figure 1 (Supplement S1).

The electrodes used to deliver IRE are 19-gauge unipolar needles inserted transperineally into the prostate gland using a tracking grid under transrectal ultrasound guidance. The electric pulsed field leads to the disruption of cell membranes and microvascular thrombosis, with resultant cellular death with respect to inert biological layers. Focal therapy for prostate cancer using IRE is potentially an easy opportunity to treat clinically significant intermediate-risk lesions usually less than 2 cm in size and well characterised using multiparametric magnetic resonance imaging (mpMRI) and targeted biopsy.



Figure 1. (**A**) Electric field settings for IRE; (**B**) The halo of the therapeutic electric field covers the uncertainty of the location of the tumour edge (blue) on the mpMRI image.

Six key rules to conduct focal ablation of localised prostate cancer using IRE:

- 1. The shape of the area bounded by the needles (probes) should completely cover the tumour area and a safety margin (IRE ablation zone) of at least 0.5 cm.
- 2. The therapeutic electric field halo covers the uncertainty between the mpMRI image and the pathological edge of cancer, which is estimated at around 1 cm to cover 100% of tumour margins.
- 3. The recommended distance between two probes should be less than 2.5 cm and over 0.8 cm.
- 4. The probes should be as far away as possible from sensitive anatomical structures such as the rectal wall or neurovascular bundles.

- 5. The exposed part of the needle should be between 1.0 and 2.5 cm in length and adapted to the curvature of the edge of the prostate gland, to reduce the impact of the electric field outside of the prostate.
- 6. The axis of the needles, particularly their active tip length, must be strictly parallel.

3. Relevant Sections

3.1. Surgical and MRI of Prostate Anatomy in the Context of IRE

To effectively manage prostate tumours with IRE, high-quality imaging of the prostate is essential. Before the procedure, detailed cartography and measurement of the lesion are required to determine the optimal placement of the needles that will cover the entire tumour area (volume) while ensuring the safety of critical anatomical structures such as the rectum, urethra, bundles of nerves (*cavernous nerve*) and sphincter muscle.

The prostate is a fibromuscular acinar gland located in the pelvic region (Figure 2). It is shaped like an inverted curved cone. It is located from its cranial (base) to its caudal (apex) part, respectively between the bladder neck on its upper side and the triangular ligament of the pelvic floor and the *levator ani muscle* which is covered by the endopelvic fascia on its lower side. Its anterior border is related to the pubic symphysis, separated by a fatty space (retropubic fat space of Retzius) and a venous plexus (venous plexus of Santorini). Its posterior border is closely related to the rectum and is separated by a continuous layer at the posterior surface of the prostate and the seminal vesicles ("fascia rectoprostatica") usually known as Denonvilliers' fascia. The anterior surface of the prostate apex is partially covered by the external urethral sphincter muscle which extends caudally enveloping the membranous urethra. On the postero-lateral sides, the gland is connected to the neurovascular bundles which are associated with the vascular pedicles that penetrate it and are bordered by the cavernous autonomic nerves of the lower hypogastric plexus. Neurovascular bundles are more antero-laterally located when they come near the apex [8]. The shape of the prostatic apex is more or less prominent in front or behind the membranous urethra and has been identified from MRI anatomical views by Lee SE et al. [8]. The prostate is crossed by the urethra and the ejaculatory ducts which join the urethra at the *colliculus seminalis*. The urethra shows an intraprostatic flexion, designed as U open forward (110–140°) which bends at the colliculus seminalis [9,10] (Figure 2). Proximally between the bladder neck and the colliculus seminalis the axis of the urethra is globally inclined downwards. Distally, it is inclined upwards. So, on the axial transrectal echography view the urethra section moves along this U line. From the *colliculus seminalis* to the apex, the urethra is surrounded by smooth muscle fibres and elastic fibres. The glandular groupings that make up the prostate define different zones histologically, generally described according to Mac Neal's segmentation into an anterior fibromuscular stroma (SMA), a posterolateral peripheral zone, a periurethral transition zone and a central zone wrapping the ejaculatory ducts [11] (Figure 2).

Prostate cancer occurs more frequently in the peripheral zone of the prostate (70%) than in the transitional zone (25%) or the SMA zone (5%), this difference is explained by the density of glands susceptible to transformation in each zone. Usually, in the axial plane, partial removal of prostate cancer involves a focal area that covers at least the tumour area and its safety margin of 5 mm and at most a lateral or transvesical (anterior or posterior to the urethra) half ablation. The different zones are recognisable on the anatomical T2 MRI sequence [12] (Figure 2). The anatomy and its structural aspects and the contours of its borders evolve with aging according to the increase in size related to the benign hyperplasia of the transition zone.

T2 weighted anatomical sequences in axial and sagittal planes are used to model the placement of the needles. These planes enable precise measurements of the tumour and the distance to neighbouring critical structures, as shown in Figure 3A,B. These measurements need to be customized to the individual size and shape of the prostate [13].



Segmentation Frontal plane



Segmentation Sagittal plane



Segmentation Axial plane (A)



3D Perineal view, Tumour (green) in left prostatic lobe



(B)

Figure 2. (**A**). Segmentation of the prostate and pelvic organs. (**B**). Three-dimensional (Visible Patient Planning 1.0.18; Strasbourg, France) from T2 weighted images were acquired with a 3 Tesla MR imaging system (Siemens Healthcare, Erlangen, Germany) using a 32-channel phased-array torso coil according to a standardized protocol.

Indeed, the individual variability of the size of the prostate (Supplement S2 related to benign prostate hyperplasia in the transition zone changes the curves of the intraprostatic urethra curve and the prostate's edge for low to high prostate volumes (Figure 4). As such, these measurements need to be tailored to the individual characteristics of the patient's prostate to ensure the most effective and safe IRE procedure possible.



(A)



Figure 3. The maximal length of the tumour and safety margin area must be contoured at multiple different levels from the base to the apex of the prostate and must be totally integrated into the predicted ablation area. (**A**) Axial view endmarks; (**B**) Sagittal view endmarks. Posterior edge of the prostate (yellow), anterior wall of the rectum (red).



(A)



Figure 4. (**A**) Changes of the posterior curve edge of the prostate in parasagittal view of the prostate according to the prostate volume ((**left**): Prostate Volume: 30 cc; (**Middle**) 55 cc; (**right**): 80 cc). Yellow line posterior edge of the prostate. Red line: curve of the rectum and anal canal. (**B**) Adjust the length of the bare active part of the needles to the curve of the posterior edge of the prostate gland to avoid damage to the rectal wall. Green light is safe; Red light is dangerous.

3.2. Placement of the Needles on the Axial Prostatic View

On axial view the prostate is a circular or elongated ovoid shape with an inward curve or indentation on its back side in front of the rectum. Sometimes a large prostate means that the pubic arch may limit access to anterior needles insertion. Therefore, the extended lithotomy position (nutation movement in the sacroiliac joint) increases the pelvic outlet. Tumour area must be contoured on the different levels from the base to the apex of the prostate. The longest size of the tumour in the axial plan is measured, it could integrate the different levels of the tumour in the prostate gland (Figure 3A).

The average estimated uncertainty between mpMRI and histology has been estimated to approximately 3–5 mm [14,15]. However, according to the individual variability, Le Noblin et al. report that a 9 mm treatment margin would be optimally applied to the non-capsular margin to achieve complete histological tumour destruction in 100% of patients [16]. The tumour surface visible on the MRI and the virtual safety margin expected must be covered by the therapeutic electric field halo around the active part of the needles

(Figure 1B). This is because the therapeutic electric field halo around the lines between the electrodes extends outwards by around 5 mm (Supplement S1)

The construction of the necessary shape covering the expected ablation area in the axial plan could be easily based on a combination of equilateral or right-angled triangles.

To simplify the strategy of electrode placement, we suggest the formation of an equilateral triangle with borders of 2 cm in length (or two right-angled triangles joined A: 1.73 cm; B: 1.0 cm; C: 2.0 cm). The surface of IRE ablation for an isosceles triangle with 2 cm by side between three needles is 1.7 cm^2 . The surface area with a diameter of 2 cm is 3.14 cm^2 (PI cm²). The basic configuration of needle placement is, therefore, either an equilateral triangle (all angles are at 60°) or a right-angled triangle. The possible dimensions of right-angled triangle legs (*cathetus*), according to the Pythagorean formula, are given in Supplement S3 for a range of hypotenuse dimensions between 1 and 2.0 cm.

The line between the first two inserted needles usually bridges the tumour, with the maximal distance possible between the two needles being 2.0 to 2.5 cm. For right-angled triangles, the maximal length is the hypothenuse border. Therefore, a tumour with a diameter < 5 mm and <10 mm could be readily covered by one and two triangles, respectively, with the longest border being 2 cm (Supplement S4)

Tumours > 10 mm in size (Figure 5) require more complex configurations, allowing the areas of different triangles to be totally covered by the therapeutic electric field. The combination of triangles could be adapted to the treatment situation, with respect to a distance between any two needles being <2.5 and >0.8 cm. The number and arrangement of the triangles are determined by the size and shape of the tumour. IRE requires the use of between three to six needles, and treatment with only two needles is not recommended. Different situations and tumour sizes or forms are illustrated in Figure 5. Insertion of the electrodes into the tumour tissue is possible, but Nickfarjam A et al. [17] point out that these configurations can significantly increase thermal damage due to the high electrical conductivity present. The triangles are constructed with the placement of the other needles abiding the minimal (0.8 cm) and the maximal (2.5 cm) distance between any two electrodes and, if possible, along the edge of the prostate gland if the tumoural area is close.



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Figure 5. Cont.



Figure 5. Modelling of 3 clinical situations with different tumour sizes and shapes. (**A**) Case 1: (**B**) Case 2; (**C**) Case 3. Tumour shape (blue); dotted red lines define distance between needles.

After the placement of the needles, the relative distances are checked, along with the active electric pathways which need to be open or excluded to cover the tumour, whilst avoiding redundant electrical pathways (Figure 5). If a high electric field or pulse length is used near the thermal effect zone (Thermal effects > 50 °C can occur along the probes for higher voltages (>2500 V) [18]. (Figure 1), the probes can potentially heat up; therefore, they should be as far away as possible from sensitive anatomical structures such as the rectal wall, urethra or neurovascular bundles.

3.3. Placement of the Needles on the Sagittal View

The baso-apical length of the tumour determines the necessary length of the active part of the needle. The needles should be tilted by 10–15° in the sagittal plane to follow the rectal angle and to allow the visualisation of the posterior baso-apical edge basal of the prostate gland without excessive deformation. If necessary, by adapting the inclination of the bony pelvis. The axis of the needles, in particular their active length, must be strictly parallel. The exposed part of the needle should, therefore, be between 1.0 and 2.5 cm in length and adapted to the curved edge of the prostate gland. Indeed, the impact of the electric field outside of the prostate must be avoided, especially in front of the rectal wall, at the level of the prostate apex (Figures 3B and 4B), to avoid the risk of the exposed active part of the needle outside of the prostate gland and close to the rectal wall causing a prostate–rectal fistula complication.

4. Conclusions and Future Directions

The management of early stage prostate cancer remains controversial, due to the risk of over- or under-treatment [19]. IRE, like other ablative technologies, has recently been applied and is currently being evaluated to mitigate the adverse effects of total treatment of early stage prostate cancer [20]. A comprehensive understanding of both the surgical and radiological anatomy of the prostate is vital for achieving successful outcomes in IRE procedures. The critical areas which limit the use of IRE are shown in Figure 6. This knowledge empowers healthcare professionals to optimise patient safety, minimise complications and maximise the efficacy of prostate cancer treatment using IRE.



Figure 6. Critical (red: to be avoid and yellow: be careful) and safe (green) areas which limit the use of IRE in axial and sagittal planes. Black anterior (pubic bone); black posterior (seminal vesicles).

Supplementary Materials: The following supporting information can be downloaded at: https://www. mdpi.com/article/10.3390/anatomia2030021/s1, S1: Configuration of an equilateral triangle using 3 needles. The therapeutic electric field around the lines between the electrodes extends outwards by approximately 5mm; S3: Table of correspondence between cathetus distances (A&B) and hypothenuse distance C; S4: Tumours with a length < 10 mm could be readily covered with simple triangular shapes; S2: Axial, sagittal and parasagittal view of prostate according to low (30cc), intermediate (55cc) and high (80cc) volumes.

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