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Step-by-Step

Cryotherapy for posterior lesions of the prostate: the hydrogel technique

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Keywords

cryotherapy, focal therapy, prostate cancer, hydrogel, rectal spacer

Introduction

While radical prostatectomy and radiotherapy have robust long-term cancer control success for localised prostate cancer, the whole-gland treatment approaches carry a certain degree of negative impact on patients' functional outcome [1]. Focal therapy targets only the cancerous foci within the prostate and thus minimises morbidity and complications. Cryotherapy as one of the most established focal therapy tools has demonstrated satisfactory oncological and functional results [2]. However, posterior lesions have been a concern for cryotherapy due to proximity to the rectum. It has been shown that while the temperature of −20°C is the threshold required to result in coagulative necrosis of tumour cells and often cryotherapy achieve a targeted temperature of −40°C, damage to surrounding healthy tissue can occur in normal tissue at −15°C [3]. Hydrogels are injectable viscous semi-liquid compounds comprised mostly of water with a hydrophilic polymer matrix giving structure to the substance. They can be polyethylene glycol (PEG) or hyaluronic acid-based products. De Castro Abreu et al. [4] have demonstrated the feasibility of adopting hydrogel into cryotherapy in a cadaver model by expansion of the Denonvilliers' space. In a porcine model, Lam and Ng [5] have verified the temperature insulation ability of hydrogel. In the present clinical study, we illustrate and guide the usage of the hydrogel technique in cryotherapy for posterior lesions of the prostate. We aimed to assess the feasibility of such a technique in expanding the use of cryotherapy for posterior lesions.

Step-by-Step Description of the Procedure

Cryoablation is performed with fusion software platform (Trinity® system: KOELIS, La Tronche, France). Preoperatively, the patient's MRI images are registered for subsequent fusion and ablation planning. After general anaesthesia, the patient is positioned in the Lloyd-Davies position. The perineum is shaved and prepared with antiseptic solution to facilitate subsequent hydrogel injection and cryoablation (Video S1).

Hydrogel Injection

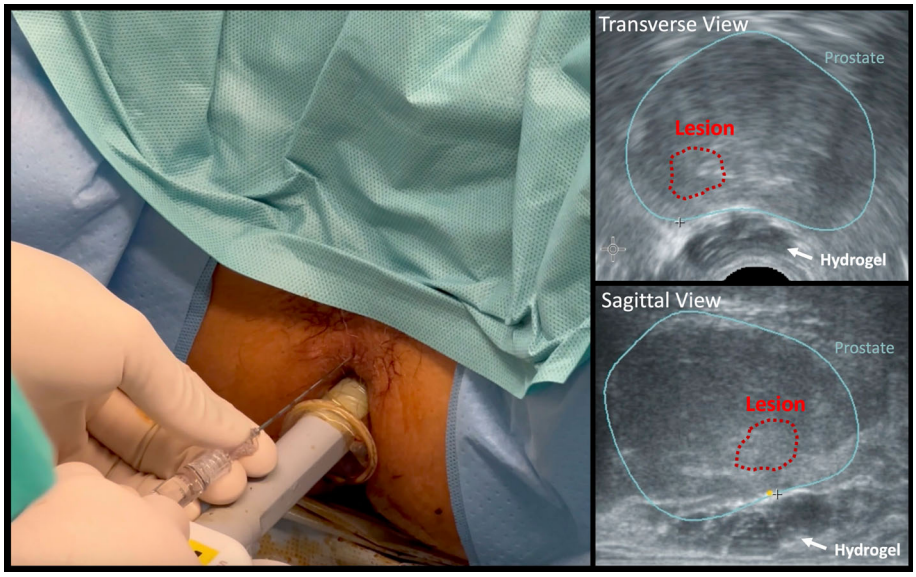
A TRUS probe is inserted into the rectum to visualise the prostate. Normal saline (10 mL) is injected by a midline puncture, through the perirectal fat under Denonvilliers' fascia, to hydrodissect and develop the plane between the prostate and rectum. Keeping the TRUS probe parallel to the posterior prostate surface will help keep the needle in the correct trajectory and increase the ease of needle visualisation. Moving the needle right to left and anterior to posterior can help ensure the needle not being in the rectal wall or prostate capsule.

Subsequently, the syringe of normal saline is replaced by hydrogel (Barrigel®; PaletteLife Sciences, Santa Barbara, CA, USA), which is injected slowly into the anterior perirectal fat while pulling the syringe backwards under continuous TRUS guidance. A total of 9 mL of Barrigel is used. Unlike the case of pre-radiotherapy spacer injection, in which we aim at delivering an even distribution of hydrogel between the prostate and rectum, in the case of focal cryotherapy one may opt for tailor-making the hydrogel distribution according to the laterality of the lesion (Fig. 1). Either way, the prostate is lifted up from the rectum, creating an extra buffer distance for subsequent ice-ball expansion.

Cryoablation

After hydrogel injection, cryoablation (ICEfx™ Cryoablation System; Boston Scientific Corp., Marlborough, MA, USA) is

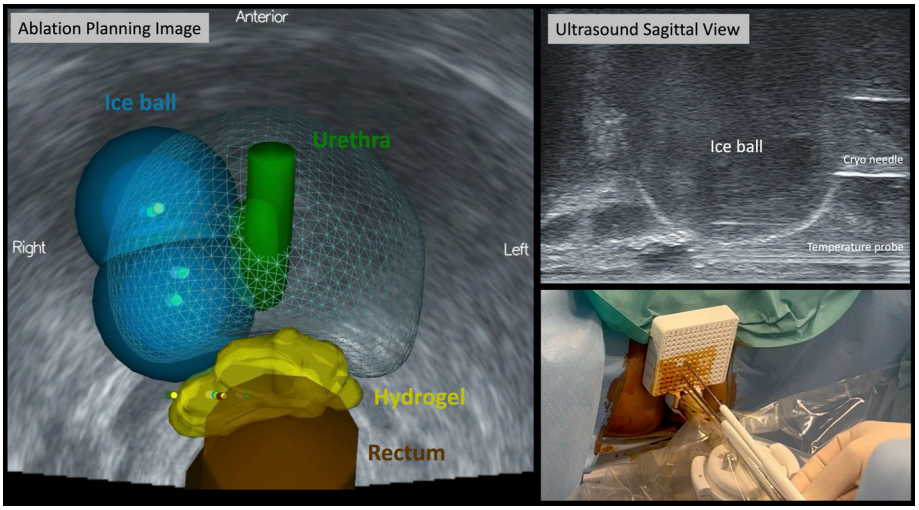
Fig. 1 Injection of hydrogel to create extra distance between the prostate and rectum, allowing the ice-ball to achieve a good margin for lesion ablation.



performed with a full-grid guidance under fusion software navigation. Contouring of the prostate and hydrogel location on TRUS images allows us to visualise the final configuration of hydrogel between the prostate and rectum during ablation planning (Fig. 2).

Once the contouring has been completed, the cryoablation needle position needs to be planned and registered. Eventual ice-ball configuration is simulated on the fusion software in order to ensure adequate ablation coverage (Fig. 2). Alternatively, as per other conventional practices of cryoablation, the cryoablation needles can be positioned free-hand without fusion software navigation. Either way, the rectum, the hydrogel and the posterior boarder of the prostate can be visualised on TRUS clearly. After urethral warmer insertion, cryoablation with two freeze–thaw cycles can be executed. Cryoablation needles used in the series were IcePearl™ 2.1 CX or IceSphere™ 1.5 X (Boston Scientific Corp.). Real-time visualisation of the ice-ball is shown on the TRUS image. With the hydrogel lifting up the prostate from the rectum, the most posterior part of the ice-ball boundary manages to go beyond the prostate capsule with a good ablation margin. At the same time, the rectum is protected.

Fig. 2 Fusion software simulation image and real-time TRUS image during cryoablation, demonstrating the ice-ball can expand beyond the prostate capsule.



Temperature probe within hydrogel in front of the rectum ensures a temperature >0°C.

A urethral catheter is inserted after cryoablation is completed. Trial without catheter (TWOC) is done on postoperative Day 2 or Day 7 according to individual surgeon's discretion. Before TWOC, patients go home with a catheter valve in order to minimise the inconvenience from a urine bag.

Outcome

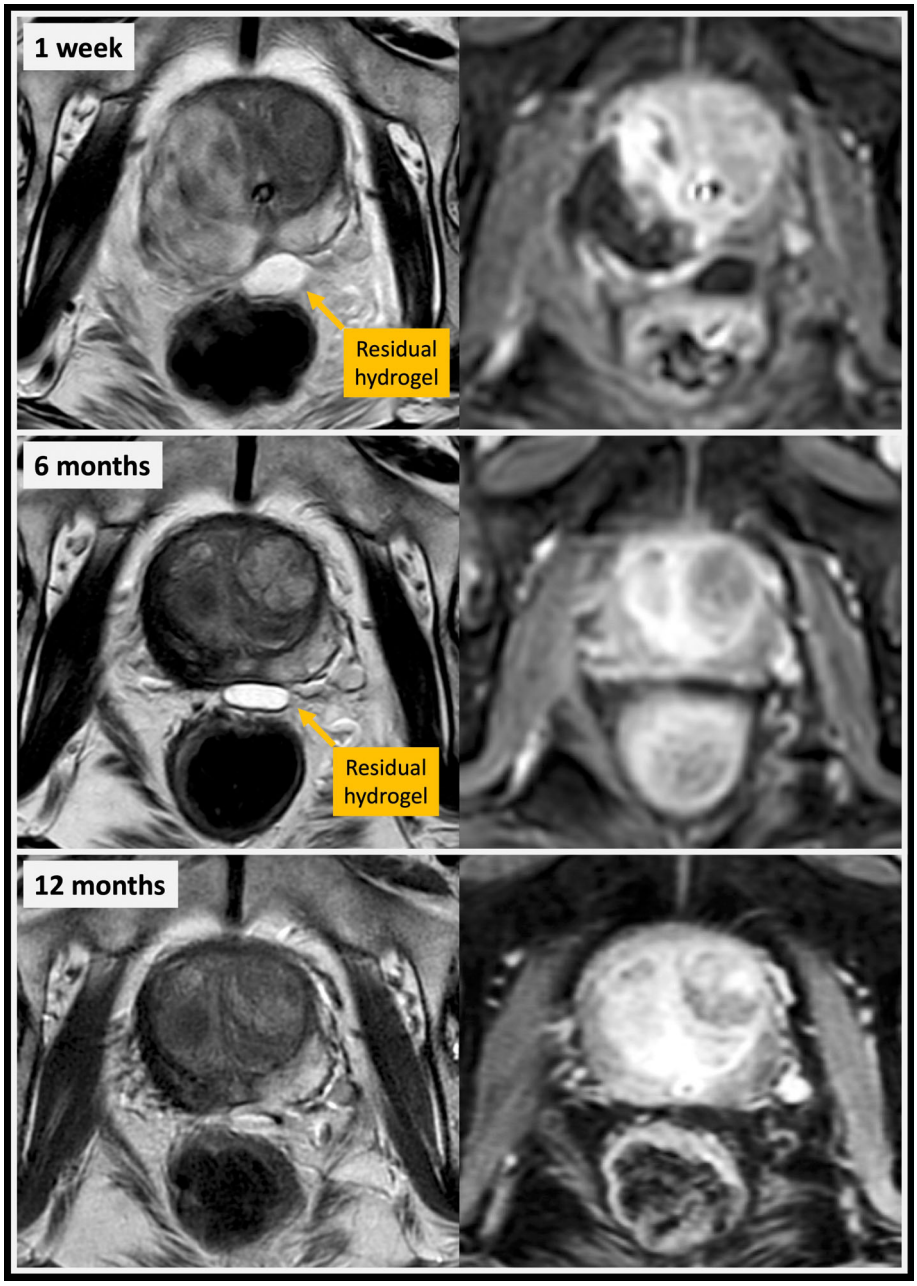
Between June 2023 to May 2024, 10 patients with middle or posterior lesions in their prostate going for cryotherapy were recruited for hydrogel injection in two academic units (Table S1). All patients were consented to the procedure and to the prospective focal therapy registry approved by our local institutes. The mean (SD) prostate size was 46.5 (24.2) mL and median (interquartile range) patient age was 72 (67.0–74.3) years. No patient was found to have any complication related to hydrogel injection or cryoablation. One patient developed Clavien–Dindo Grade IIIb complication related to his auxiliary procedure of TURP. The patient had a right posterior lesion in a 107 mL prostate gland. Due to concomitant LUTS, TURP was performed in the same session after cryoablation. The patient developed clot retention after the procedure; clot evacuation and haemostasis was performed on postoperative Day 1. The patient being on aspirin, which had not been withheld perioperatively, together with the relatively large-sized prostate, may have contributed to the occurrence of such a complication after TURP. Regarding the per protocol post-cryotherapy 1-week MRI, all patients were found to have satisfactory ablation coverage with a safe distance between the prostate and rectum maintained (Fig. 3). No complaint of tenesmus was expressed by the patients at the 3-month follow-up. The mean (SD) pre- and postoperative PSA level was 10.46 (5.48) and 4.09 (2.88) ng/mL, respectively ($P = 0.009$). There was no significant change in erectile function after the procedure. The mean (SD) pre- and postoperative 26-item Expanded Prostate cancer Index Composite (EPIC-26) sexual domain score was 49.9 (31.2) and 48.7 (20.3), respectively ($P = 0.869$). Comparing with the focal ablation of posterior lesions by high-intensity focused ultrasound (HIFU) of the same period in our institute, no statistically significant difference was observed in operative time, change in PSA level, and postoperative erectile function (Table S2).

Discussion

Focal cryotherapy is a minimally invasive method used to manage low- to intermediate-risk prostate cancer. However, its ability to reach −40°C at the prostatic capsule has always been limited by the proximity of the rectal wall. Some centres adopt the 'à la carte' approach, using focal cryotherapy for anterior lesions and saving the posterior lesions for focal HIFU [6]. Contrary to cryotherapy, HIFU is a modality of transrectal thermal energy delivery. It has the advantage of precise tissue ablation for posteriorly located lesions. However, the presence of intraprostatic calcification can affect its efficacy. Having both the availability of cryotherapy and HIFU may allow more flexibility in ablation planning. However, the 'à la carte' approach may be feasible only when the centre has the luxury of having multiple modalities of focal therapy. Cryotherapy being an established tool for prostate cancer eradication, expanding its use to include posterior lesions is a significant step to maximise the therapeutic advantage provided by such a modality.

Rosenberg et al. [7] reported their experience of 10 patients using hydrodissection to optimise the cryotherapy outcome. In their study, 10 mL saline was injected every time near Denonvilliers' fascia. Repeated injection was needed as the fluid was continuously absorbed. In their series, the saline volume used ranged from 150 to 500 mL per patient. Furthermore, the occasional presence of air bubbles obscured the view of the TRUS. Replacing saline with hydrogel can reduce the volume of agent used to create the space, as well as minimising the artefact on TRUS images. Hydrogel spacer has been shown to decrease irradiation gastrointestinal toxic effect by increasing the distance between the prostate and rectum. Taking from the experience of prostate radiation therapy, adopting hydrogel spacer as a way to expand the posterior margin during cryotherapy is a logical way to maximise the ablation success. In the *in vitro* experiment by de Castro Abreu et al. [4], a PEG hydrogel was tested and was shown to be visible on TRUS without any change in shape during cryoablation even when the core temperature inside the hydrogel had reached −15°C. In the *in vitro* study of both PEG-based spacer and hyaluronic acid-based spacers, Lam et al. [5] reported that macroscopically both types of spacers had minimal alternation in shape by ice-ball compression during the freeze cycle. However, it was noted that hyaluronic acid-based spacer had a better cold insulation property, which may be accounted for by the relatively higher water content in the PEG-based spacer. In our experience, hyaluronic acid-based hydrogel achieves a satisfactory space creation as evidenced by intraoperative TRUS confirmation, as well as a good temperature insulation as evidenced by intraoperative temperature monitoring. Furthermore, postoperative MRI images have demonstrated stable configuration of hydrogel after cryotherapy. Concerning the potential impact of residual hydrogel on subsequent secondary treatment for recurrence, Crisostomo-Wynne et al. [8] reported on the feasibility of robot-assisted radical prostatectomy after hydrogel injection even with increased scarring around the tissue. However, its impact on repeated focal therapy treatment has not been investigated yet. While

Fig. 3 Post-cryotherapy MRI images (left: T2 sequence; right: contrast sequence) at 1 week, 6 and 12 months.



more data are needed to assess the long-term implications of spacer injection, the hydrogel technique as a technical modification for posterior lesion cryoablation potentially gives room for a better posterior margin during prostate focal therapy.

Conclusions

Focal cryotherapy has been shown to be a reliable tool in the focal therapy armamentarium. Our findings demonstrate that hydrogel can serve as an essential adjunct in focal cryotherapy. The hydrogel technique is a reliable way to create more space between the prostate and rectum in order to achieve an adequate ablation coverage for posterior lesions. This potentially can improve both oncological outcomes and patient safety. Further study is needed to verify if the potential advantages of this resultant wider margin can be sustained in the long term.

Disclosure of Interests

The authors have no conflicts of interest to declare.

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Abbreviations: HIFU, high-intensity focused ultrasound; PEG, polyethylene glycol; TWOC, trial without catheter.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Patients characteristics.

Table S2. Comparison between cryoablation with the hydrogel technique and HIFU focal ablation for posterior lesions.

Video S1. Cryotherapy for posterior lesions of the prostate: the hydrogel technique.

