Focal treatments for prostate carcinoma: MR patterns after Focal Cryotherapy and Focal Brachytherapy

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Learning objectives

To report the spectrum of MR findings of prostate gland treated with focal cryotherapy and focal brachytherapy.

To illustrate MR imaging effectiveness in the early evaluation of post-implant dosimetry in patients treated with focal brachytherapy.
Background

Althoght prostate cancer has been considered a heterogeneous, multifocal disease requiring whole-gland therapy, recent studies demonstrated that a proportion of cancers are unifocal, unilateral or of lower malignant potential, and focal therapy for prostate cancer is emerging as a desirable and feasible approach for low-risk, localized disease (1).

The essence of focal therapy is precise targeted ablation of a small tumors, preferably minimally invasively, while preserving the remainder of the uninvolved organ (1,2,3,4,5).

Cryosurgery is one option for the treatment of localized prostate cancer that provides some advantages over the conventional treatments (low morbidity rate, shorter hospital stay, negligible blood loss, less expensive than competing therapies).

Brachytherapy is another option for the treatment of localized prostate cancer that provides some advantages over the conventional treatments (low morbidity rate, shorter hospital stay, preservation of potency), and focal brachytherapy, currently being used in breast cancer therapy, can be utilized in the treatment of select patients with low-to-moderate risk prostate cancer as a possible alternative to whole-gland treatment (6).

The soft-tissue contrast resolution and multiplanar imaging capability of MR provide an effective tool for imaging follow-up of neoplastic lesions treated with focal cryotherapy and focal brachytherapy.
MATERIALS AND METHODS

FOCAL CRYOTHERAPY

Six patients with localized prostatic carcinoma underwent Focal Cryosurgical Ablation.

The planning of the treatment was based on byoptic and preoperative MR imaging evaluation of size and position of the neoplastic lesions.

All cryoablation procedures were performed using four cryoprobes (SeedNet, Galil Medical) (Fig. 1). Cryoprobes were placed percutaneously, using endorectal sonography guidance, with the aid of a needle-spacing template (Fig. 1, Fig. 2).

Patients were treated with hemiablation in five cases (the freezing zone enclosed half of the prostate parenchima with a margin of about 5 mm, taking care of the periurethral zone in order to spare the urethra; the ablation zone was extended to include ipsilateral neurovascular bundle and margin, for the treatment of possible extracapsular extension of disease). In one case we treated only the lesion, located in the central gland (Fig. 3).

The development of the ice ball was controlled under ultrasound evaluation (Fig. 2, Fig. 4).

Patients were followed up clinically, biochemically and by MR imaging 24 hours after surgery, and subsequently after 3, 12 and 24 months.

All examinations were performed with a 1.5T MR system (Philips Gyroscan Intera Power) using the body phased-array coil. Imaging protocol included axial Gradient Echo (GRE) T1w, Turbo Spin Echo (TSE) T2w sequences and contrast-enhanced (ce) TSE fat-suppressed (FS) T1w sequence. TSE T2w and ce TSE T1w images were also obtained in the sagittal and coronal planes. Post contrast TSE FS-T1w images were evaluated before and after digital subtraction procedure.

We evaluated the following parameters: A. Morphology of the gland; B. Signal intensity of the treated areas; C. Patterns of vascularization of the treated areas.

FOCAL BRACHITHERAPY

5 patients with localized prostatic carcinoma underwent Focal Brachytherapy.

The planning of the treatment was based on byoptic and preoperative MR imaging evaluation of size and position of the neoplastic lesion. Seeds were placed...
percutaneously with perineal approach, using endorectal sonography guidance, with the aid of a needle-spacing template (Fig. 5).

Ablation zone is extended to include ipsilateral neurovascular bundle and margin (treatment of possible extracapsular extension of disease) (Fig. 6, Fig. 7).

Patients were followed up clinically and biochemically (PSA). MR imaging follow-up was performed at 30 days and 12 months after therapy. 24hours after the treatment a radiographic evaluation of the pelvis was performed in all the patients, to evaluate number and position of radioactive seeds (Fig. 8).

30 days after the treatment a morphological MR study was performed for post-implant dosimetric evaluation, using a 1.5T MR system (Philips Gyroscan Intera Power). The post-plan dosimetries were based on unenhanced T1w (to locate the radioactive sources) and T2w (to visualise the prostate) imaging, obtained using a phased-array body coil (Fig. 9). Post-implant dosimetry was estimated on fused transverse T1w and T2w MR images: a dedicated Treatment Planning System (Variseed 7.0, Varian) with an image fusion software, was used to perform dosimetry (Fig. 10, Fig. 11).

12 months after treatment was performed a MR imaging follow-up with a 1.5T MR system (Philips Gyroscan Intera Power) using the endorectal coil. All the patients underwent MR conventional multiplanar Turbo Spin-Echo (TSE) T2w sequences, followed from dynamic axial contrast enhanced (ce) Gradient-Echo (GRE) T1w sequence.

On MR images performed 30 days after the treatment we evaluated the morphology of the gland, the seeds position and the post implant dosimetry. On MR images performed 12 months after the treatment we evaluated the morphology and the patterns of vascularization of the gland.

**IMAGING FINDINGS**

**FOCAL CRYOTHERAPY**

Twenty-four hrs after treatment the treated areas were about 10 mm larger than the original gland (Fig. 12, Fig. 13, Fig. 14, Fig. 15). MR examinations showed a mean decrease in size of the treated areas of 30% after 3 months, 70% after

Twenty-four hours after cryoablation, T2w images showed the prostate parenchima heterogeneously iso-hyperintense, without significative differences between the treated and the spared zone of the gland. The margins of the gland came out as poorly defined, without perilesional rim (Fig. 12, Fig. 13, Fig. 14, Fig. 15).

After 3, 12 and 24 months follow-up treated tissue showed high signal intensity on T2w images, with a sharp hypointense perilesional rim (Fig. 14, Fig. 15). All the patients
showed persistence of isointensity of the spared prostatic tissue. The margins of the gland in correspondence of the treated areas resulted well defined Fig. 14, Fig. 15).

Post treatment ce-FS T1w and subtracted ce-MR images showed ischemia of the treated zone of the gland, hypointense as compared with normal prostatic parenchyma, and relative enhancement of the untreated gland (Fig. 12, Fig. 13, Fig. 14, Fig. 15, Fig. 16).

CLINICAL FOLLOW-UP

All the patients had a stable PSA level (range 0.2-1.4 ng/mL) 24 months after the treatment. No patient had clinically documented urinary complications related to the procedure. MR imaging follow-up revealed no evidence of local or nodal recurrence in all the patients.

FOCAL BRACHITHERAPY

In all the patients, a radiographic evaluation of number and position of radiation therapy seeds was performed at 24 hrs after the treatment (Fig. 8).

30 days after treatment, prostate resulted more than 5 mm larger than the original gland (Fig. 9) on morphologic T1w and T2w MR images (Fig. 5). MR examinations showed a mean decrease in size of the gland of 50% at 12 months after the treatment (Fig. 17)

30 days after focal brachytherapy procedure, T2w images showed the prostate parenchima heterogeneously iso-hyperintense, without significative differences in terms of signal intensity between the treated and the spared zone of the gland. The margins of the gland resulted poorly defined, without perilesional rim (Fig. 9). Radiation therapy seeds were seen on GRE T1w image as small focal signal intensity voids (Fig. 9, Fig. 10, Fig. 17, Fig. 18).

At 12 months imaging follow-up, MR evaluation showed reduction in size of the gland, with diffuse reduction in signal intensity on T2w images and contrast enhancement on dynamic ce GRE T1w images of the treated areas, due to parenchimal fibrosis and atrophy. All the patients showed persistence of isointensity of the spared prostatic tissue. The margins of the treated areas resulted poor defined (Fig. 17).

CLINICAL FOLLOW-UP

PSA level decreased in all the patients at 12 months after the treatment (mean PSA level 2,2 ng/mL). No patients had clinically documented urinary complications related to the procedure. MR imaging follow-up revealed no evidence of recurrence in all the patients.
Fig. 1: FIG. 1 (Cryoprobes and cryoablation procedure of a prostatic carcinoma) (A) 17G cryoneedle. (B) scheme of cryoprobes placement into the prostate gland, using endorectal sonography guidance and the aid of a needle-spacing template.

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Fig. 2: FIG. 2 (Cryoablation procedure of a prostatic carcinoma) (A) 17G cryoneedles inserted through the perineum. Ultrasonographic evaluation of cryoneedle position, to outline the shape of the prostate (B,C). Development of the iceball under ultrasound control, on axial (D) and longitudinal (E,F) planes.

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**Fig. 3:** FIG. 3 (Focal cryoablation of a prostatic carcinoma) Schemes of prostate ablation using Focal Cryoablation technique. We used the B technique in five cases (ablation zone includes ipsilateral neurovascular bundle and margin) and the A technique (ablation of the lesion only) in one case, located in the central gland.

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**Fig. 4:** FIG. 4 (Focal hemiablation of a prostatic carcinoma) Scheme of probe position using Focal Cryoablation technique (A). Development of the iceball under ultrasound control (axial plane, B)

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**Fig. 5:** FIG. 5 (Radiation therapy seeds and Brachytherapy implant procedure) Radiation therapy seeds (A). Seeds mounted on dedicated needle (B). Seeds placed percutaneously, using endorectal sonography guidance, with the aid of a needle-spacing template (C,D). Pre-treatment planning (E). Ultrasonographic evaluation of the prostate after the implant (F)

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Fig. 6: FIG. 6 (Focal Brachytherapy of a prostatic carcinoma) Schemes of prostate ablation using Focal Brachytherapy technique. We used the B technique (Ablation zone is extended to include ipsilateral neurovascular bundle and margin, for the treatment of possible extracapsular extension of disease).

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Fig. 7: FIG. 7 (Focal Brachytherapy of a prostatic carcinoma) Percutaneous positioning of the seeds, using an endorectal sonography guidance, with the aid of a needle-spacing template (A). Ultrasonographic pre-planning of the treatment (B)
**Fig. 8:** FIG. 8 (Focal Brachytherapy of a prostatic carcinoma) Radiographic evaluation of number and position of Radiation therapy seeds, performed 24 hrs after the treatment.

**Fig. 9:** FIG. 9 (Focal Brachytherapy of a prostatic carcinoma) Transverse GRE T1w (A) and TSE T2w (B) MR images of 3-mm-thick section for 3D reconstruction of the performed implant. Radiation therapy seeds were seen on GRE T1w axial (A) and sagittal (C) MR images as small focal signal intensity voids, while the anatomy of the gland was well visualised on TSE T2w image MR (B).
Fig. 10: FIG. 10 (82-year-old man who underwent Focal Brachytherapy of a prostate carcinoma of the left peripheral zone) Transverse GRE T1w MR image at 30 days after the implant. Radiation therapy seeds are seen as small focal signal intensity voids (A). Post-implant dosimetry based on fused transverse GRE T1w and TSE T2w MR images (B) obtained 30 days after the treatment.

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Fig. 11: FIG. 11 (Focal Brachytherapy of a prostatic carcinoma) Post-implant dosimetry based on fused transverse GRE T1w and TSE T2w MR images. The yellow lines
represent the isodose line of the reference dose. Radiation therapy seeds were seen as red dots.

Fig. 12: FIG. 12 (73-year-old man who underwent hemi-cryoablation for prostatic carcinoma) On T2w images, treated prostate showed heterogeneous iso-hyperintensity 24 hrs after treatment prostate, and was more than 5 mm larger than the original gland (B,C). Conventional and subtracted ce-T1w MR images showed ischemia of the left portion of gland (arrows), and relative enhancement of the periurethral zone and contralateral portion of the gland (D,E,F).
Fig. 13: FIG. 13 (47-year-old man who underwent hemi-cryoablation for prostatic carcinoma) MR images obtained before treatment showed an enhancing neoplastic nodule in the right portion of the prostate (A,B,C, arrow). On T2w images, treated prostate showed heterogeneous iso-hyperintensity 24 hrs after treatment (D). Subtracted ce-T1w MR images showed ischemia of the cranial right portion of gland (arrows), and relative enhancement of the periurethral zone and contralateral portion of the prostate (E,F).

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Fig. 14: FIG. 14 (73-year-old man who underwent hemi-cryoablation for prostatic carcinoma) MR images obtained before treatment showed an enhancing neoplastic nodule in the left portion of the prostate (white arrows). On T2w images, treated prostate was heterogeneously iso-hyperintense 24 hrs after treatment. Cryolesion resulted hyperintense, with hypointense perilesional rim (yellow arrows), 3, 12 and 24 months after treatment, with isointensity of the spared zone of the gland. 24 hrs after treatment, the prostate was about 1 cm larger than the original gland; progressive decrease in size at the following controls. Conventional and subtracted ce-T1w MR images showed ischemia of the treated area (red arrows), and relative enhancement of the periurethral zone and contralateral portion of the prostate.

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**Fig. 15:** FIG. 15 (72-year-old man who underwent focal-cryoablation for prostatic carcinoma) Prostate tumor, located in the right central gland (white arrows). On T2w images, treated prostate was enlarged and heterogeneously iso-hyperintense 24 hrs after treatment. Cryolesion resulted hyperintense, with hypointense perilesional rim, 12 and 24 months after treatment (yellow arrows). Progressive decrease in size of the treated area during the follow-up. Conventional and subtracted ce-T1w MR images showed ischemia of the treated area (red arrows), and relative enhancement of the periurethral zone and contralateral portion of the prostate.

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**Fig. 16:** FIG. 16 (comparison between whole gland and focal cryoablation) MR images showed ischemia of the peripheral gland and relative enhancement of the central portion of the prostate, due to the sparing of the periurethral zone, in a patient treated with whole gland cryoablation. Ischemia of the left portion of the gland, with relative enhancement of the spared zone of the gland, in patient treated with focal (left) cryoablation.

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**Fig. 17**: FIG. 17 (77-year-old man who underwent Focal Brachytherapy of a prostate carcinoma of the left peripheral zone: MRI follow-up) Axial TSE T2w (A) and sagittal GRE T1w (B) MR images 30 days after treatment. MR evaluation performed at 12 months after the treatment showed reduction in size and signal intensity on T2w images (C,D) and reduction of contrast enhancement on dynamic conventional (E) and subtracted (F) ce GRE T1w images of the treated portion of the gland (arrows), due to parenchimal fibrosis and atrophy.

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Fig. 18: FIG. 18 (Prostate carcinoma: comparison between whole gland and focal brachytherapy) GRE T1w MR images and post-implant dosimetry based on fused transverse MR images: comparison between whole gland (A,B) and focal (C,D) brachytherapy

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Conclusion

DISCUSSION

FOCAL CRYOTHERAPY

Cryosurgery is the term used to describe tissue destruction using extreme cold temperature. The histologic sequelae of this process are inflammatory reaction, coagulative necrosis and finally fibrosis and scarring (9).

Focal cryoablation is an alternative therapy for the treatment of localized prostate cancer, that provides precise targeted ablation of small tumors, preserving the remainder of the uninvolved organ (3,4) (Fig. 16).

As it is not possible to document histopathologically the complete tissue necrosis after cryoablation, while PSA level comes out as bouncing and therefore not completely useful in the follow-up, a radiological follow-up can be helpful (8).

Among the different imaging techniques, MRI represents the ideal one since it is reproducible, non operator dependent and optimally able to detect the difference between necrotic and still viable tissue. Nevertheless, usefulness of MR imaging follow-up of patients with prostate cancer treated with cryosurgery remains controversial (5,6,7,8).

In patients treated with focal cryoablation for localized prostate cancer, cryolesions typically appear to be hyperintense with a hypointense peripheral rim on T2w images, due to the coagulative necrosis induced by cryotherapy. The treated areas showed an increase in size 24 hours after treatment, due to postcryosurgery prostate edema, and a progressive decrease in size in the following controls, due to fibrotic evolution of cryolesions. After focal ablation, prostate showed no significant vascularization of the treated zone, while the periuretral and controlateral zone were spared, on ce-MR images, due to vasocostriction and thrombosis of distal arterioles and venules induced by cryotherapy.

In our study, according to previous MR imaging studies performed on patients treated with cryotherapy for small renal masses (10), the most significant MR patterns in the follow up of prostatic carcinoma treated with cryosurgical focal ablation were the decrease in size with the passing of time and the complete ischemia of the treated area of the prostate, while the periuretral and controlateral zone were spared.

The most effective MR techniques for lesions sizing and enhancement evaluation were TSE T2w and subtracted ce-TSE-FS T1w sequences.

FOCAL BRACHITHERAPY
Permanent low dose-rate brachytherapy has been recognised to be an alternative therapeutic option to radical prostatectomy as well as to conformal radiotherapy in patients with clinically localised carcinoma (7), and recently focal brachytherapy was proposed in the treatment of select patients with low-to-moderate risk prostate cancer as a possible alternative to whole-gland treatment (6) (Fig. 18).

As it is not possible to document histopathologically the efficacy of the treatment and PSA level results variable in the follow-up, a radiological follow-up can be helpful (8).

Among the different imaging techniques, MRI represents the ideal one since it is reproducible, non operator dependent and able to detect the presence of still viable tissue.

MR imaging resulted an effective technique in the in the post implant dosimetric evaluation (Fig. 6). MR imaging can also recognize the changes induced from the treatment. In our study, morphologic MR evaluation showed reduction in size of the treated area of the gland and diffuse reduction of signal intensity on T2w images due to parenchimal fibrosis and atrophy. Dynamic ce MR evaluation showed reduction of the vascularization of the gland. Radiation therapy seeds were seen as small foci of focal signal intensity void (Fig. 17).

**CONCLUSIONS**

Our medium term experience suggests that focal cryoablation and Focal Brachytherapy are safe, well tolerated and minimally invasive therapies for localized prostatic carcinoma, and MR can be an effective imaging technique in the follow-up of prostatic tumors treated with focal cryoablation and Focal Brachytherapy.

MR can be effective after focal cryoablation in the early evaluation of the effectiveness of the treatment (immediate feedback about size and geometry of the cryoinsult), in the evaluation of possible complications and in the evaluation of patients with clinical or laboratory suspect of recurrence.

MR can be also an effective imaging technique in the follow-up of prostate tumors treated with Focal Brachytherapy, in particular in the evaluation of post-implant dosimetry. MR imaging can also play a role in the evaluation of patients with clinical or laboratory suspect of recurrence.
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