FOLLOW-UP RM DOPO TRATTAMENTO

Dott.ssa Anna Damascelli
Dott.ssa Silvia Ravelli

After treatment follow-up

Treatment commonly includes:

- radical prostatectomy (RP)
- radiation therapy (RT): external-beam RT (EBRT) or brachytherapy
- prostate-sparing focal therapy: laser technology, microwave ablation, cryotherapy, or high-intensity focused ultrasound (HIFU)

Disease recurrence:

- 40% of patients after definitive treatment
- BCR predicts locally recurrent disease in up to 2/3 of patients
- PSA nadir achieved after each treatment option differs

After treatment follow-up

Recommendations	GR
In asymptomatic patients, disease-specific history and serum PSA measurement supplemented by DRE are recommended for routine follow-up. These should be performed at 3, 6 and 12 months after treatment, then every 6 months until 3 years, and then annually.	B
Imaging to detect local recurrence is only recommended if it affects treatment planning. Biopsy is usually not necessary before second-line therapy, except after EBRT when local salvage treatment is considered.	B
Routine bone scans and other imaging are not recommended in asymptomatic patients if there are no signs of biochemical relapse. In patients with bone pain or other symptoms of progression, re-staging should be considered irrespective of serum PSA level.	B

DRE = digital rectal examination; GR = grade of recommendation; LE = level of evidence; PSA = prostate-specific antigen; RP = radical prostatectomy.

European Association of Urology

Guidelines on

Prostate Cancer

N. Mottet (Chair), J. Bellmunt, E. Briers (Patient Representative), R.C.N. van den Bergh (Guidelines Associate), M. Bolla, N.J. van Casteren (Guidelines Associate), P. Cornford, S. Culine, S. Joniau, T. Lam, M.D. Mason, V. Matveev, H. van der Poel, T.H. van der Kwast, O. Rouvière, T. Wiegel

6.10.4.6 Guidelines for imaging and second-line therapy after treatment with curative intent

Biochemical recurrence (BCR) after RP	LE	GR
In the case of BCR, bone scan and abdominopelvic CT should be performed only in patients with a PSA level > 10 ng/mL, or with high PSA kinetics (PSA-DT < 6 mo or a PSA velocity > 0.5 ng/mL/mo) or in patients with symptoms of bone disease.	3	A
A Choline PET/CT is not recommended in patients with BCR and a PSA-level < 1 ng/mL	3	A
Biochemical recurrence after RT		
In patients with BCR who are candidates for local salvage therapy, prostate mpMRI may be used to localise abnormal areas and guide biopsy.	3	C

BCR = biochemical recurrence; CT = computed tomography; GR = grade of recommendation; LE = level of evidence; mpMRI = mutiparametric magnetic resonance imaging; PET = positon emission tomography; PSA-DT = prostate specific antigen doubling time; RP = radical prostatectomy; RT = radiotherapy.

After-RP follow-up

PSA should drop to undetectable levels within 2 weeks to 3 weeks

Patients should be followed with serial serum PSA measurements

BCR: PSA ≥ 0.2 ng/mL, followed by a second confirmatory serum PSA

After RP the recurrent PCa volume is estimated to be <1 cm^3 for PSA levels <3.5 ng/mL

Role for imaging

local recurrence → salvage local therapy (RT)

false positive BCR → spare pts from side effects and toxicities

distant metastasis → spare pts from side effects and toxicities

Stephenson AJ, Kattan MW, Eastham JA, et al. Defining biochemical recurrence of prostate cancer after radical prostatectomy: a proposal for a standardized definition. J Clin Oncol 2006;24(24): 3973–8.
Boccon-Gibod L, Djavan WB, Hammerer P, et al. Management of prostate-specific antigen relapse in prostate cancer: a European Consensus. Int J Clin Pract 2004 Apr;58(4):382-90.

After-RP follow-up: imaging the recurrence

Routine imaging procedures are not indicated in the absence of symptoms or a rising serum PSA

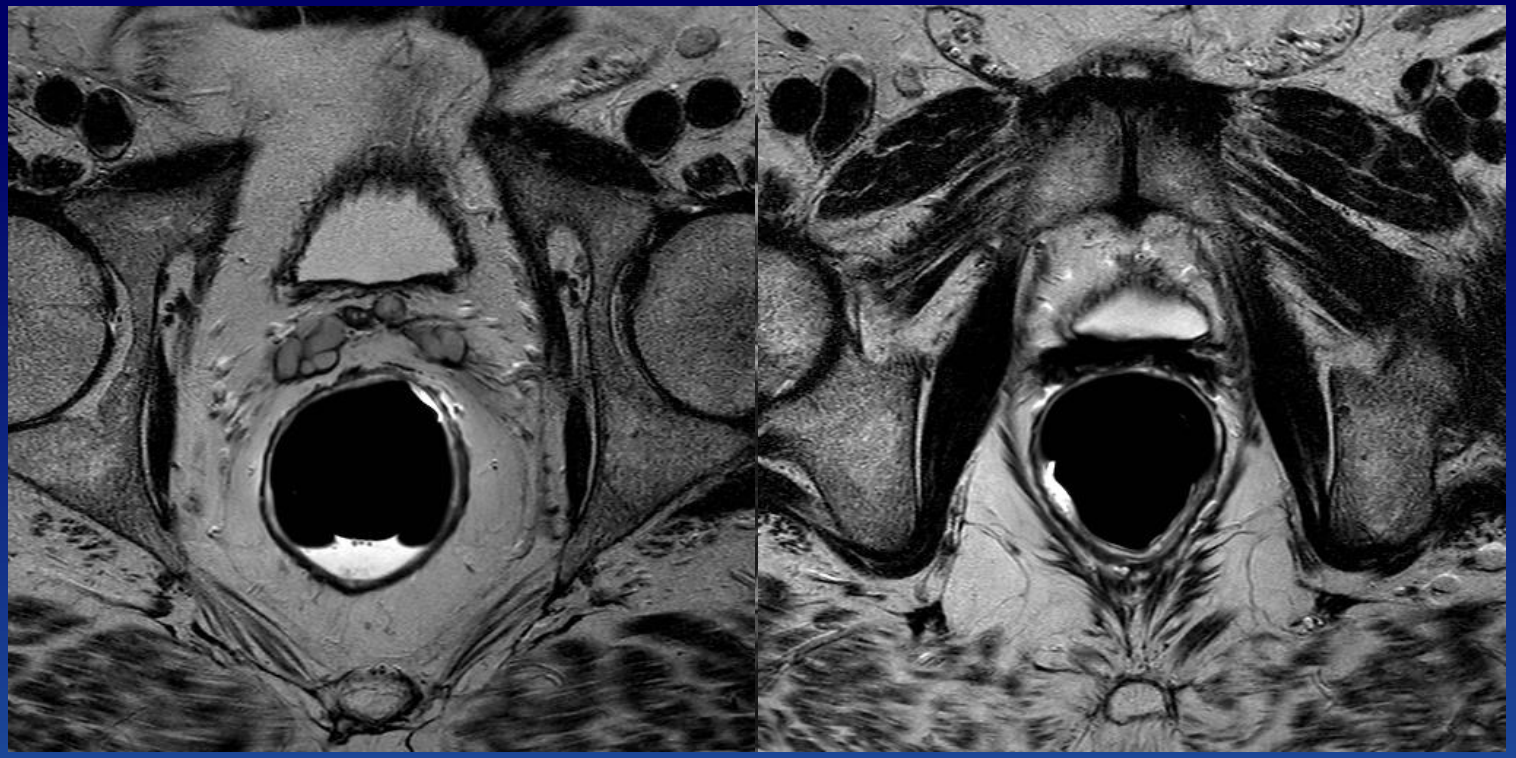
Localized	vs	Sistemic
PSA increase more than 3 years post-RP		PSA increases in less than 1 year post-RP
PSA doubling time greater than 11 mths		PSA doubling time is in 4 months to 6 mths
GS ≤ 7		GS: 8 to 10
≤ pT3a pN0, pTx , R0		pT3b, pTxp, N1
DRE TRUS mpMRI		bone scintigraphy 11C-PET/PSMA-PET CT total body

Stephenson AJ, Kattan MW, Eastham JA, et al. Defining biochemical recurrence of prostate cancer after radical prostatectomy: a proposal for a standardized definition. J Clin Oncol 2006;24(24): 3973–8.

mpMRI after-RP: TECHNIQUES

- 3T with PPA Coil or 1,5 T with Endorectal Coil
- T2w and T1w-FAT SATpost contrast axial for pelvis
- T2w HD
- Diffusion-weighted imaging (DWI) (b0 – b800 – b1600)
- ADC maps
- Dynamic Contrast Enhanced-MRI (DCE-MRI)
- Magnetic Resonance Spectroscopy Imaging (MRSI)

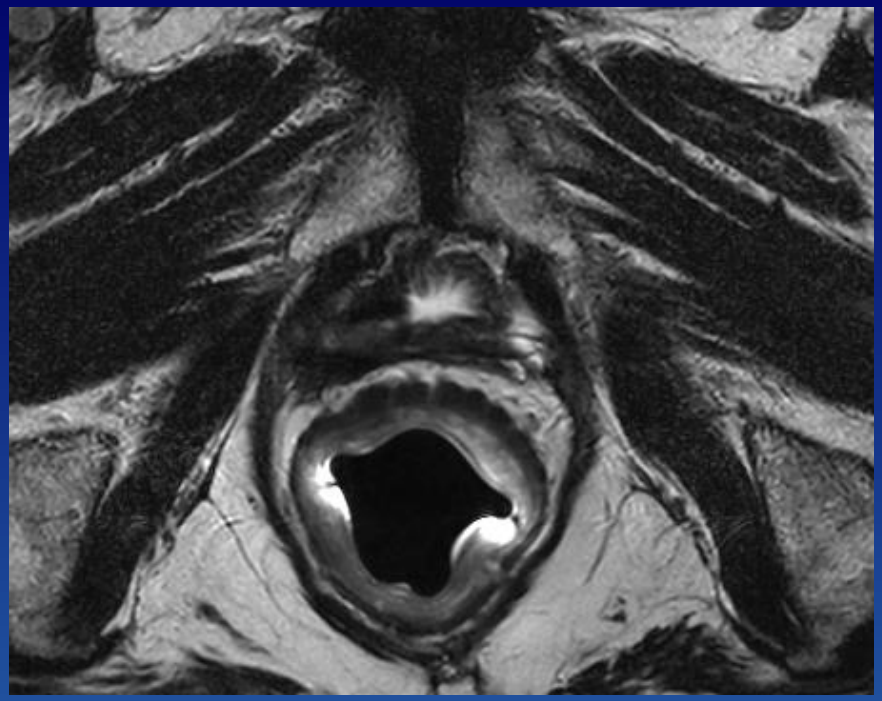
mpMRI after-RP: ANATOMICAL CHANGES



- Bladder neck
- VUA
- Thickening of Denonvilliers Fascia
- Metallic clips
- Seminal vesicles may be left (20%): presurgical locations, tubular structure
- Lymphoceles

mpMRI after-RP: local recurrence

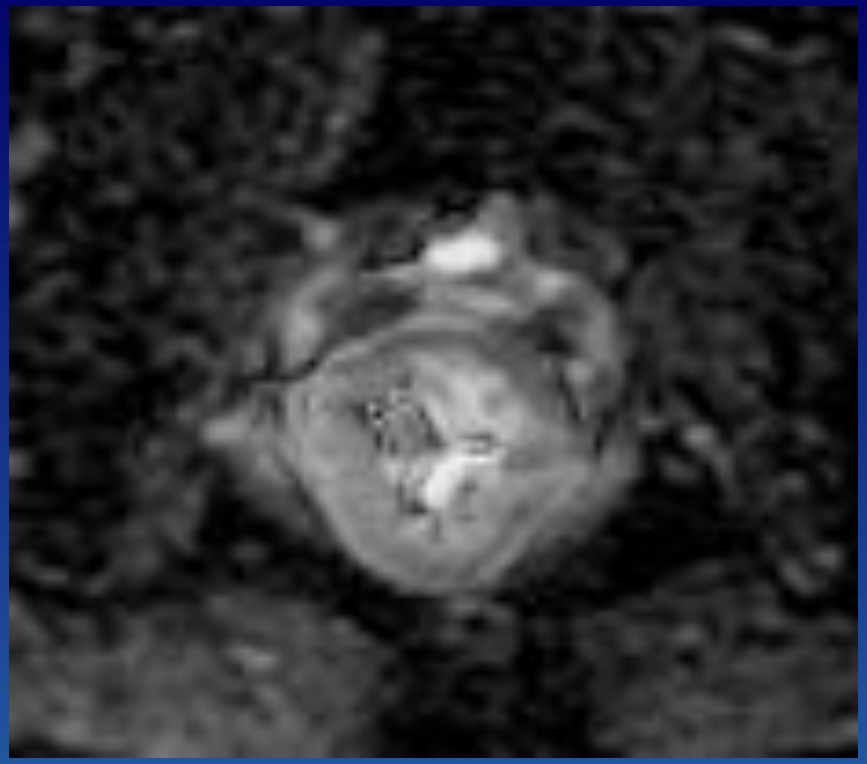
T2W



Nodular and relatively hyperintense in comparison to pelvic muscle

mpMRI after-RP: local recurrence

DWI

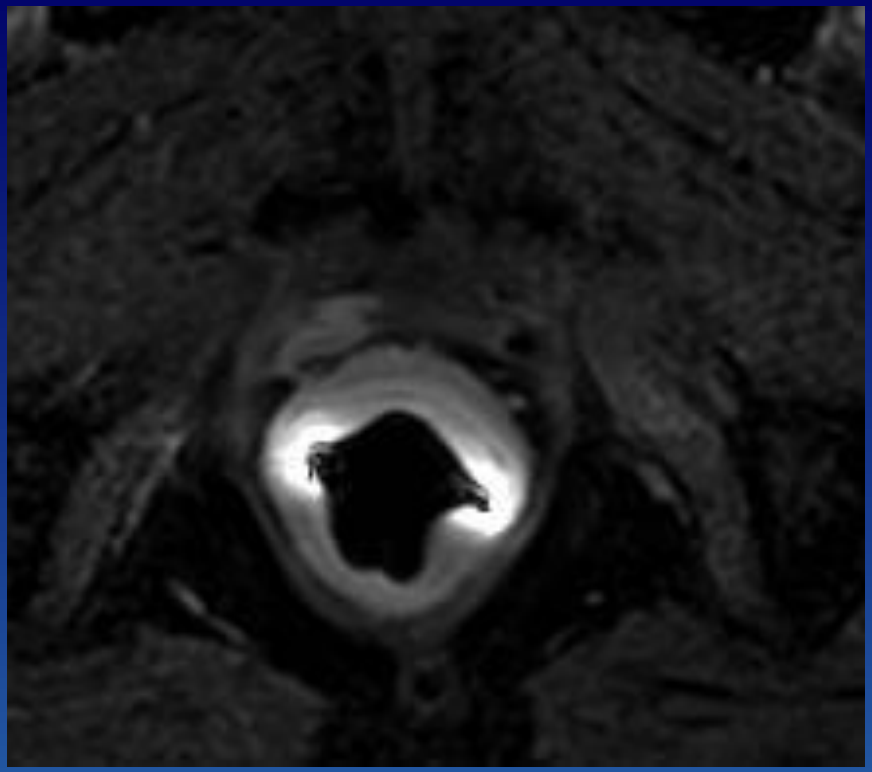


Highly dependent on whether or not surgical clips were used

May help in distinguish from mimicking etiologies (inflammation or residual benign tissue)

mpMRI after-RP: local recurrence

DCE-MRI



Hyperenhance during the arterial phase, quick washout during the venous phase

Changes in early enhancement are very sensitive for being locally recurrent disease

More reliable than DWI and has been proved as the most useful sequence for detecting recurrence

Endorectal and Dynamic Contrast-Enhanced MRI for Detection of Local Recurrence After Radical Prostatectomy

Emanuele Casciani[1]
Elisabetta Polettini[1]
Enrico Carmenini[2]
Irene Floriani[3]

OBJECTIVE. The objective of our study was to evaluate the sensitivity and specificity of endorectal MRI combined with dynamic contrast-enhanced MRI to detect local recurrence after radical prostatectomy.

MATERIALS AND METHODS. A total of 51 patients who had undergone radical prostatectomy for prostatic adenocarcinoma 10 months to 6 years before underwent a combined endorectal coil MRI and dynamic gadolinium-enhanced MRI before endorectal sonographically guided biopsy of the prostatic fossa. The MRI combined with MR dynamic imaging results were correlated with the presence of recurrence defined as a positive biopsy result or reduction in prostate-specific antigen level after radiation therapy.

RESULTS. Overall data of 46 (25 recurred, 21 nonrecurred) out of 51 evaluated patients were analyzed. All recurrences showed signal enhancement after gadolinium administration and, in particular, 22 of 24 patients (91%) showed rapid and early signal enhancement. The overall sensitivity and specificity of MR dynamic imaging was higher compared with MRI alone (88%, [95% CI] 69–98% and 100%, 84–100% compared with 48%, 28–69% and 52%, 30–74%). MRI combined with dynamic imaging allowed better identification of recurrences compared with MRI alone (McNemar test: chi-square$_1$ = 16.67; p = < 0.0001).

CONCLUSION. MRI combined with dynamic contrast-enhanced MRI showed a higher sensitivity and specificity compared with MRI alone in detecting local recurrences after radical prostatectomy.

Eur Radiol (2009) 19: 761–769
DOI 10.1007/s00330-008-1174-8

UROGENITAL

Endorectal magnetic resonance imaging at 1.5 Tesla to assess local recurrence following radical prostatectomy using T2-weighted and contrast-enhanced imaging

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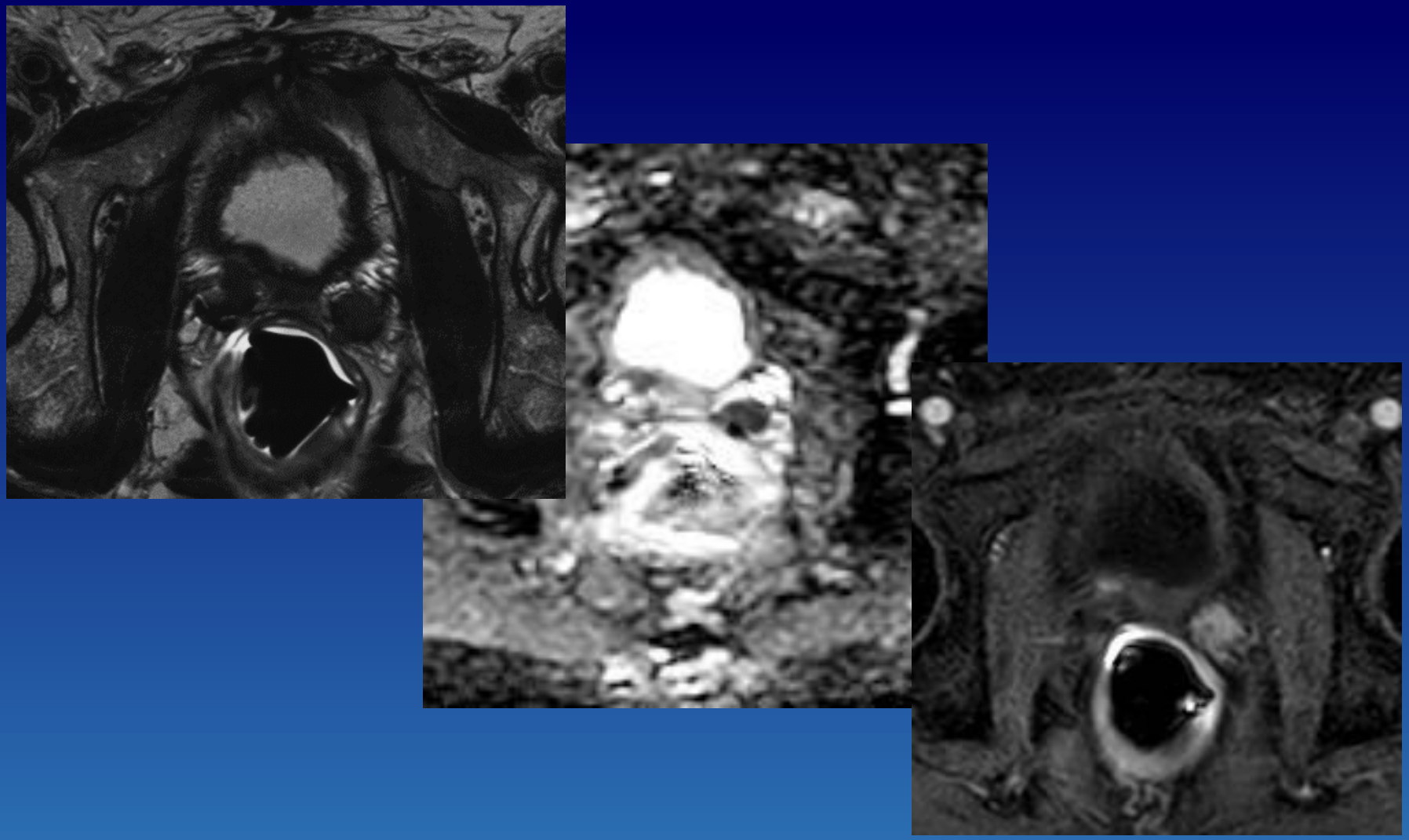
Abstract To evaluate diagnostic performance of endorectal magnetic resonance (eMR) for diagnosing local recurrence of prostate cancer (PC) in patients with previous radical prostatectomy (RP) and to assess whether contrast-enhanced (CE)-eMR improved diagnostic accuracy in comparison to unenhanced study. Unenhanced eMR data of 72 male patients (mean of total PSA: 1.23±1.3 ng/ml) with previous RP were interpreted retrospectively and classified either as normal or suspicious for local recurrence. All eMR examinations were re-evaluated also on CE-eMR 4 months after the first reading. Images were acquired on a 1.5-T system. These data were compared to the standard of reference for local recurrence: prostatectomy bed biopsy results; choline positron emission tomography results; PSA reduction or increase after pelvic radiotherapy; PSA modification during active surveillance. Sensitivity, specificity, predictive positive value, negative predictive value and accuracy were 61.4%, 82.1%, 84.4%, 57.5% and 69.4% for unenhanced eMR and 84.1%, 89.3%, 92.5%, 78.1% and 86.1% for CE-eMR. A statistically significant difference was found between accuracy and sensitivity of the two evaluations (χ^2=5.33; p=0.02 and χ^2=9.00; p=0.0027). EMR had great accuracy for visualizing local recurrence of PC after RP. CE-eMR improved diagnostic performance in comparison with T2-weighted imaging alone.

Keywords Magnetic resonance imaging · Prostatic neoplasm · Prostatectomy · Local neoplasm recurrence · Contrast media

mpMRI after-RP: local recurrence



mpMRI after-RP: PITFALLS

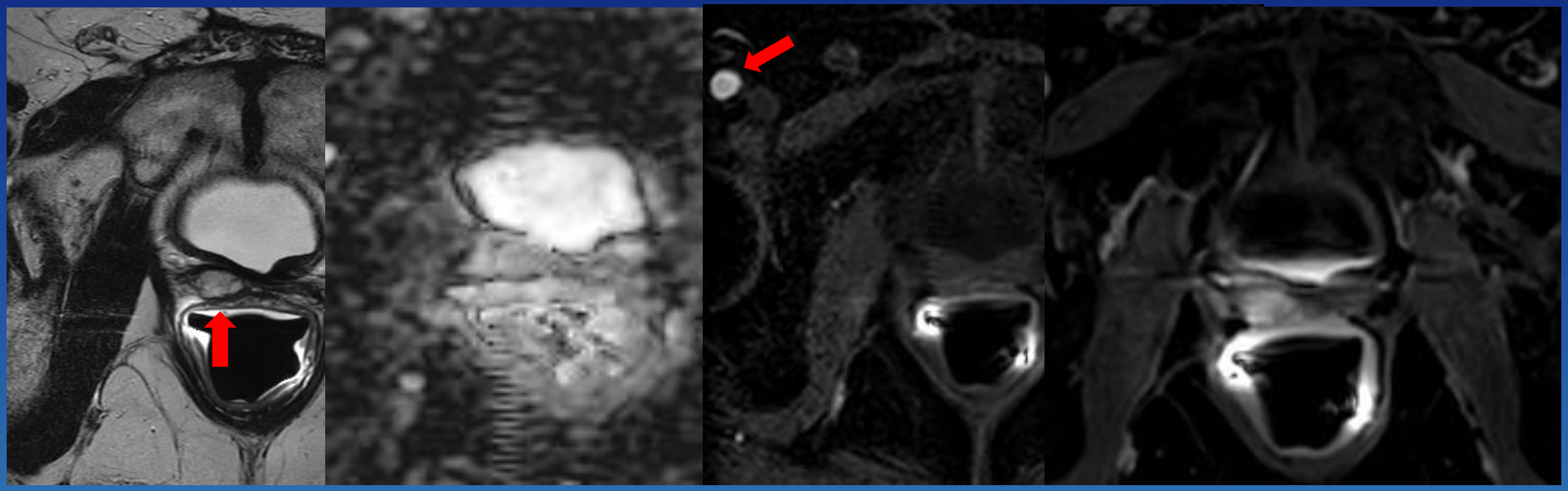
- Residual glandular tissue postsurgery

→ PSA-producing: doubling time should be much longer than for recurrent disease

➢T2W: nodular appearance resembling Pca

➢**DWI**: should not have any signal abnormality

➢**DCE**: should not enhance early in the arterial phase



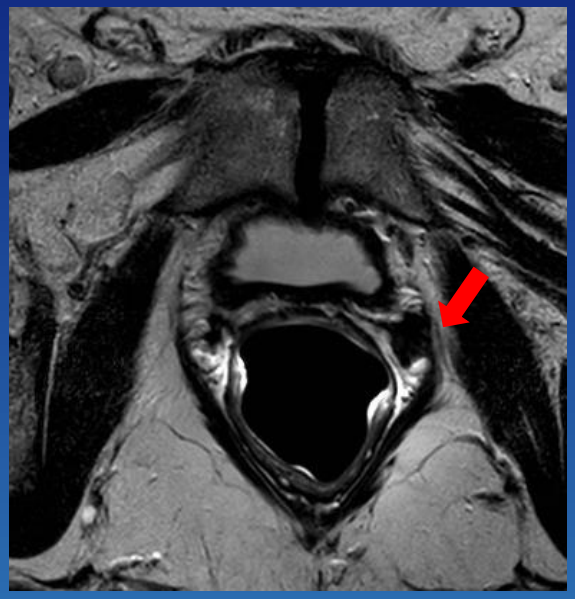
mpMRI after RP: pitfalls

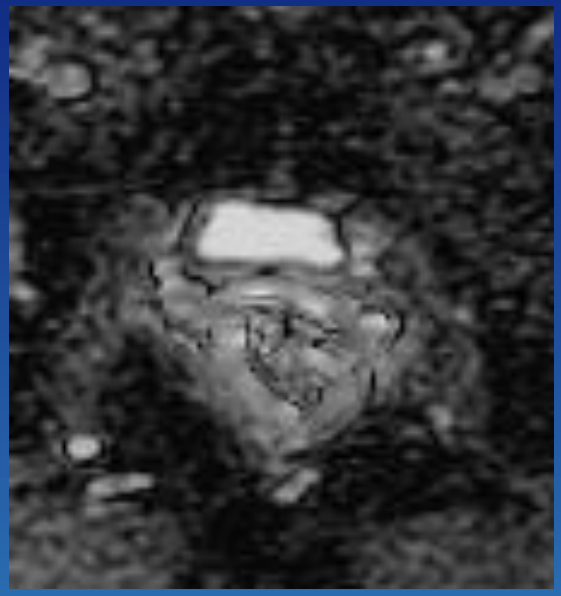
- Fibrosis

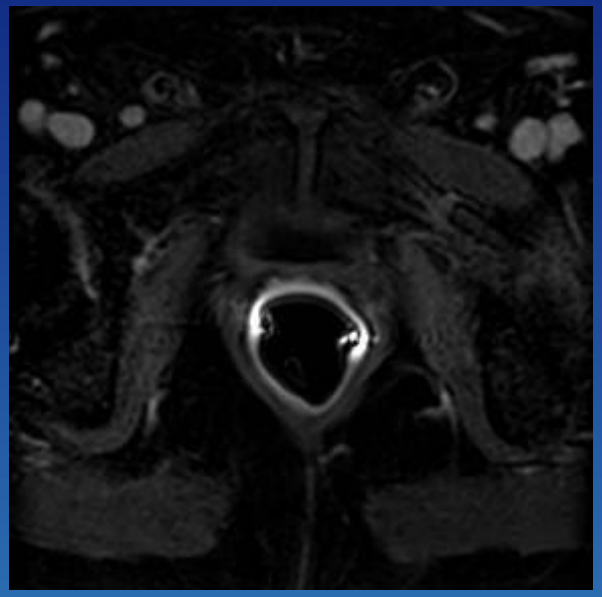
➢**T2**: more hypointense than recurrent tumor

➢DWI: restriction due to high cellularity

➢**DCE**: delayed thin layer of enhancement during the venous phase







mpMRI after-RP: PITFALLS

- Granulation tissue near VUA

T2: hyperintense (similar to recurrent tumor)

DWI: should not have any signal abnormalty

DCE: hyperenhances on an early DCE phase due to hypervascularity

- Retained seminal vescicles

- Prominent periprostatic venous pleuxus

After RT follow-up

- **EBRT** (earlier-stage disease) or **brachytherapy** (low-grade disease and in smaller prostates) or **combination** of both (high-grade diseas)
- may be combined with **hormonal therapy** to shrink the prostate for maximal treatment efficacy
- The **method** of radiation delivery and the incorporation of **hormones** in treatment are important considerations for **post-treatment imaging**

PSA nadir approximately after 18 mths (up to 3 yrs)

PSA bounce may occur at 9 to 21 mths and lasts for several months

Once nadir is established patient should be followed with serial serum PSA

BCR: 2 successive measurements showing a rise in serum PSA >= 2 ng/mL above the nadir

Roach M 3rd, Hanks G, Thames H Jr, et al. Defining biochemical failure following radiotherapy with or without hormonal therapy in men with clinically localized prostate cancer: recommendations of the RTOG-ASTRO Phoenix consensus conference. Int J Radiat Oncol Biol Phys 2006;65(4):965–74.

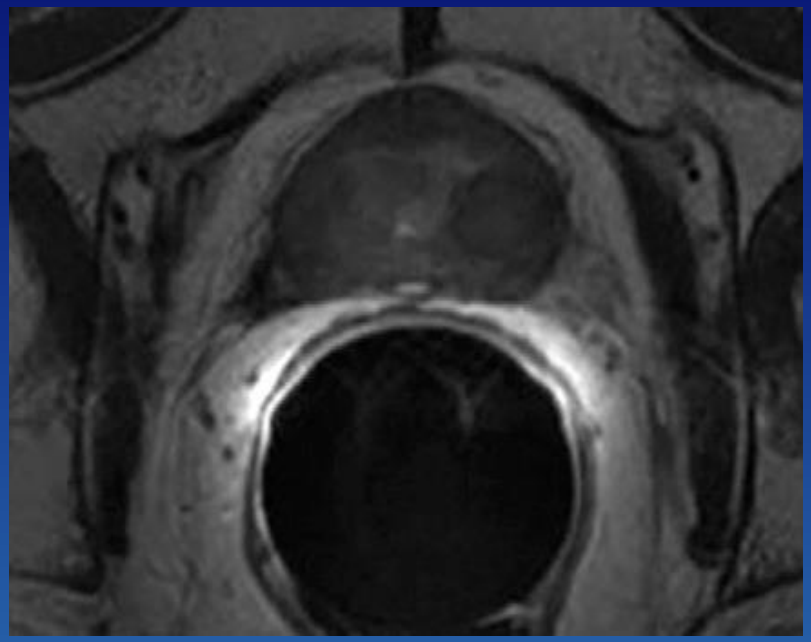
After RT follow-up

- Localized vs sistemic: less established risk factors compared with RP
- Biopsies: not routinely racommended, false negative and false positive (first 1-2 yrs)
- Imaging goal: recurrence identification→ targeted or whole gland salvage therapies (focal therapy or RP)
- Majority of post-RT recurrences have been shown to be local, with top site of recurrence the prostate→ mpMRI is essential
- Most commonly at the site of original tumor→ baseline mpMRI

mpMRI after EBRT: ANATOMICAL CHANGES

T2W

- irradiated prostate appears smaller (gland atrophy)
- hypointense
- difficulte to differentiate between prostatic zones



DWI

- postradiation fibrosis is less cellular

DCE

- diminished vascularity

Other changes

- seminal vesicles appears shrunken
- pelvic muscles are relatively hyperintense
- pelvic bones appear hypointense on T2W due to fatty replacement of bone marrow

mpMRI after EBRT: LOCAL RECURRENCE

T2W

- nodular structure, relatively hypointense, appear as a capsular bulge
- most commonly at the original site of the primary tumor
- T2W imaging has marked limitations (changed background signal)

DWI

- post-RT recurrence is similar to primary Pca
- focal hypointensity on the ADC map and hyperintensity on high *b*-value
- DWI +T2W vs T2W alone show great promise for DWI utility in post- RT imaging

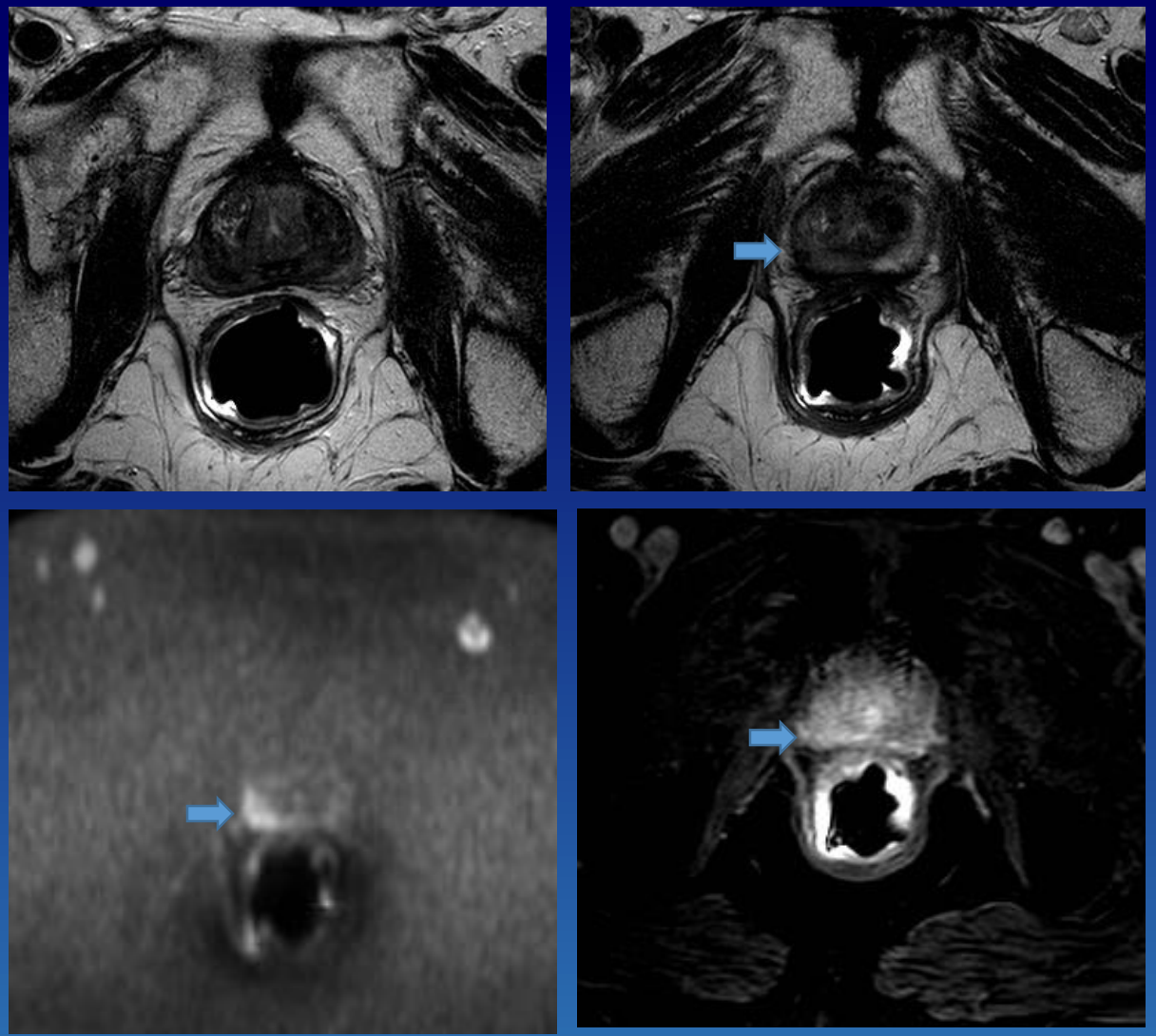
DCE

- recurrent tumors show early hyperenhancement on DCE MR imaging relative to the treated prostate
- especially powerful if it can be correlated with abnormality on T2 or DWI

MRSI

Hara T, Inoue Y, Satoh T, et al. Diffusion-weighted im- aging of local recurrent prostate cancer after radia- tion therapy: comparison with 22-core three- dimensional prostate mapping biopsy. Magn Reson Imaging 2012;30(8):1091–8.
Kim CK, Park BK, Park W, et al. Prostate MR imaging at 3T using a phased-arrayed coil in predicting locally recurrent prostate cancer after radiation ther- apy: preliminary experience. Abdom Imaging 2010; 35(2):246–52.

mpMRI after EBRT: LOCAL RECURRENCE



mpMRI after brachitherapy: ANATOMICAL CHANGES

T2W

- prostate appears smaller and hypointense (similar to EBRT)
- visualization of the radioactive seeds
- As a patient completes a brachytherapy course, the prostate gland becomes progressively more atrophic and the seeds gradually migrate peripherally

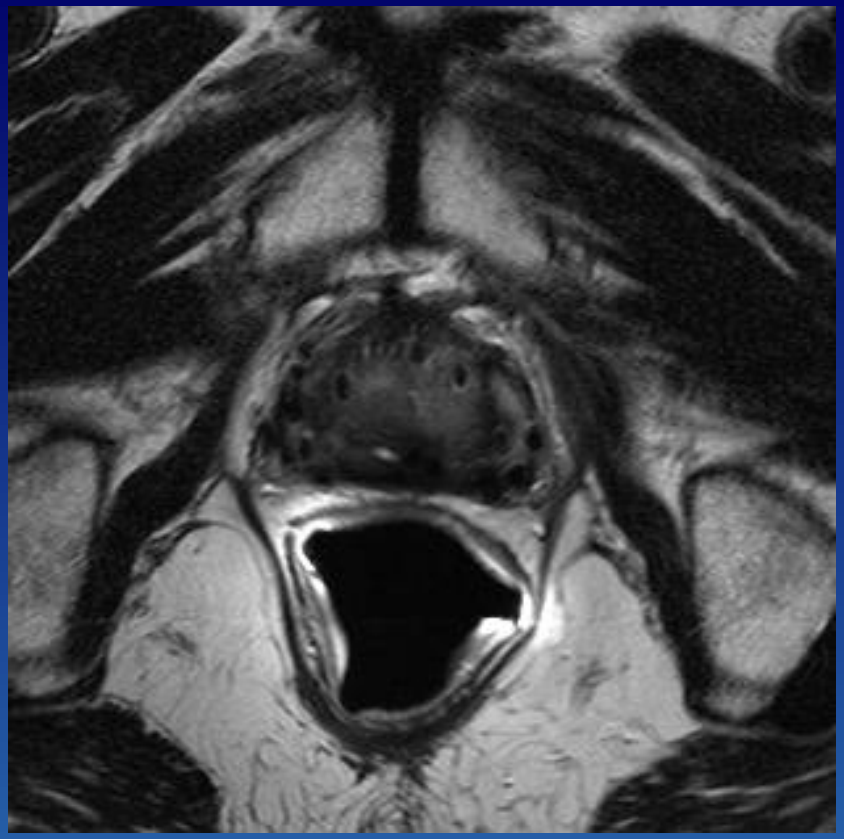
DWI

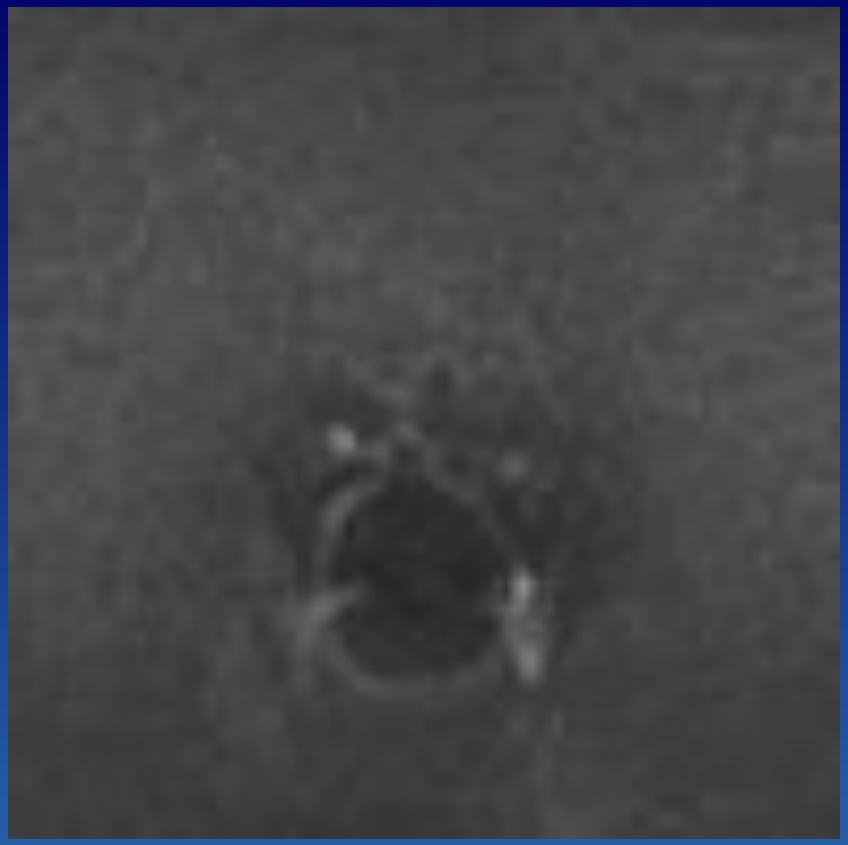
- metallic capsules introduce MR susceptibility artifacts,
- distort DWI, difficulte to evaluate

DCE

- diminished vascularity compared with pretreatment prostate tissue (similar to EBRT)

mpMRI after brachitherapy: ANATOMICAL CHANGES

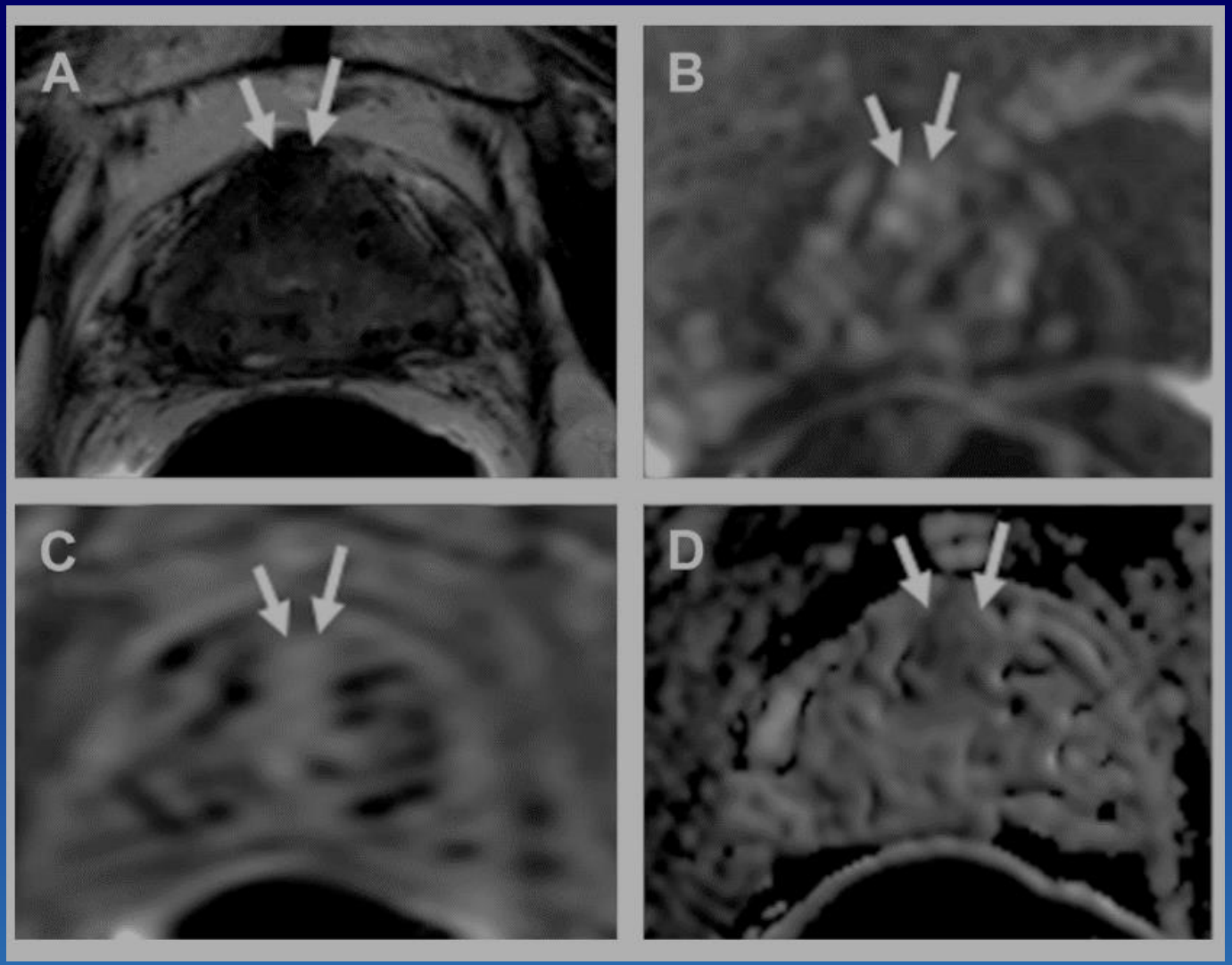




mpMRI after brachitherapy: LOCAL RECURRENCE

- recurrence is less of a concern after brachytherapy than it is after EBRT: very-low-risk primary disease
- hypointense nodule on T2W imaging that shows rapid hyperenhancement on DCE
- If DWI is not too limited, recurrent tumor appears hypointense on the ADC map and hyperintense on high *b*-value imaging

mpMRI after brachitherapy: LOCAL RECURRENCE



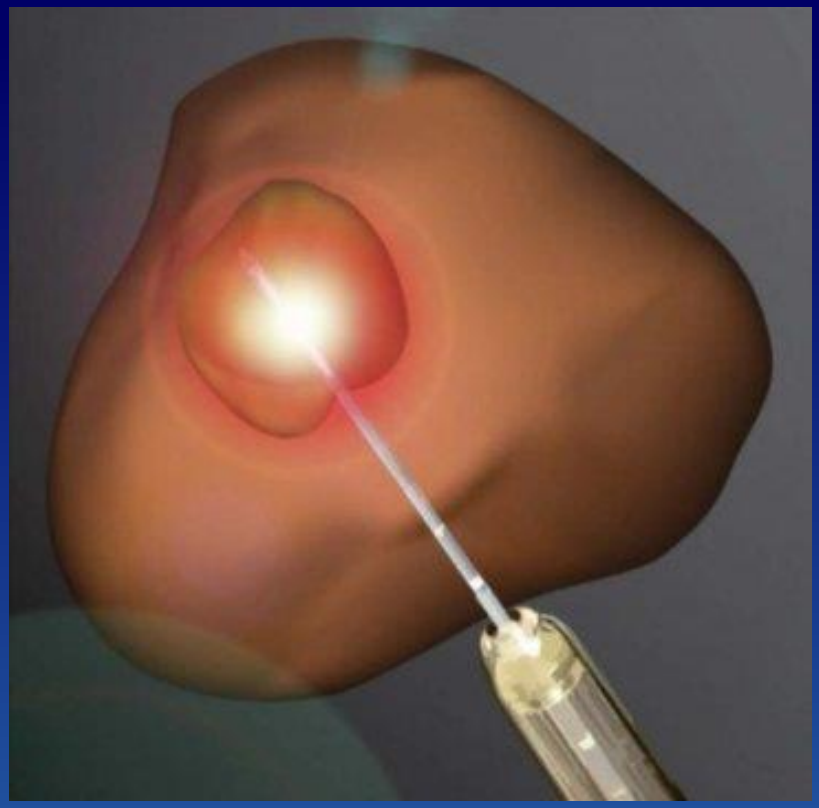
mpMRI after RT

HORMONAL THERAPY

Post-androgen deprivation: can cause additional changes to the gland and make interpretation more difficult:

the prostate shrinks in size
overall ADC values significantly increase
gland vascularity decreases

Lo scopo della terapia focale



- Distruzione cellule tumorali di una determinata area della prostata preservando la maggior parte del tessuto prostatico sano e dei tessuti adiacenti

- Scopo: ridurre effetti collaterali in termini di potenza e continenza

Caveat della terapia focale

- Ancora in fase sperimentale!! NO *standard of care*
- Non disponibili follow up a lungo termine dopo terapia focale

RAZIONALE DELLA TERAPIA FOCALE

Introduzione del dosaggio del PSA e screening opportunistico del PCa

↓

Aumento delle diagnosi di PCa

↓ ↘

Aumento trattamenti radicali (RT/prostatectomia radicale)

La maggior parte dei pazienti con diagnosi di malattia tumorale non aggressiva *(malattia a basso rischio)*

'STAGE MIGRATION'

RAZIONALE DELLA TERAPIA FOCALE

Pazienti candidabili alla terapia focale

Clinical

Clinical stage T1 or T2a
PSA < 10 ng/mL
PSA density < 0.15 ng/mL/cc^3
PSA velocity < 2 ng/mL annually for the year prior to the diagnosis

Biopsy

Minimum 12 cores
No Gleason grade 4 or 5
Maximum percentage of tumor in each core: 20%
Maximum extent of tumor in each core: 7 mm
Maximum percentage of cores affected by the tumor: 33%

Scott E. Eggener. Peter T. Scardino et al. J Urol 2007

Clinically Localized Prostate Cancer: AUA/ASTRO/SUO Guideline. Part I: Risk Stratification, Shared Decision Making, and Care Options

7. Clinicians should recommend active surveillance as the best available care option for very low risk localized prostate cancer patients. (Strong Recommendation; Evidence Level: Grade A)

12. Clinicians should inform low risk prostate cancer patients who are considering focal therapy or HIFU that these interventions are not standard care options because comparative outcome evidence is lacking. (Expert Opinion)

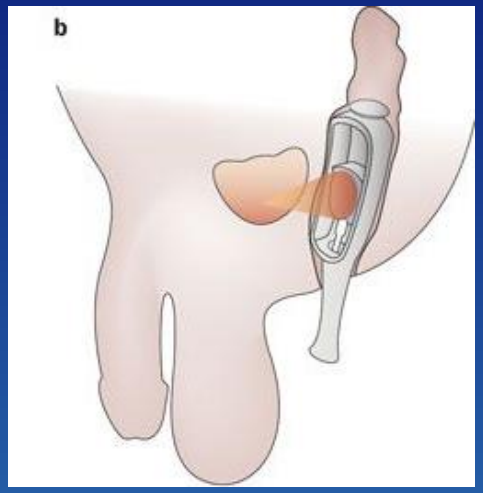
Sanda MG et. al. J Urol 2018

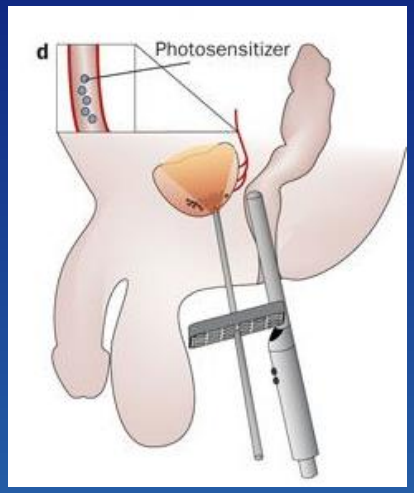
Techniques

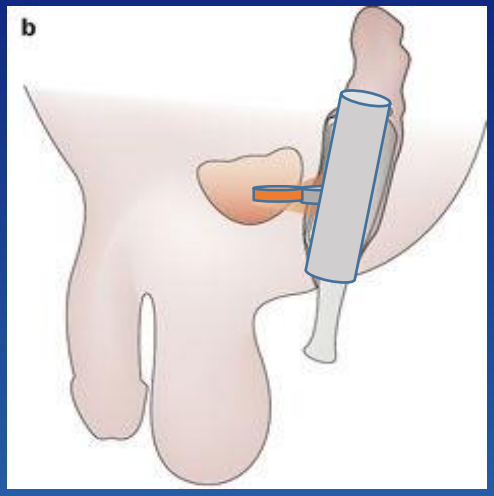
- Cryotherapy
- HIFU (high intensity focused ultrasound)
- IRE (irreversible elettroporation)
- VTP (vascular Photodynamic therapy)
- FLA (focal laser ablation)

Image guidance

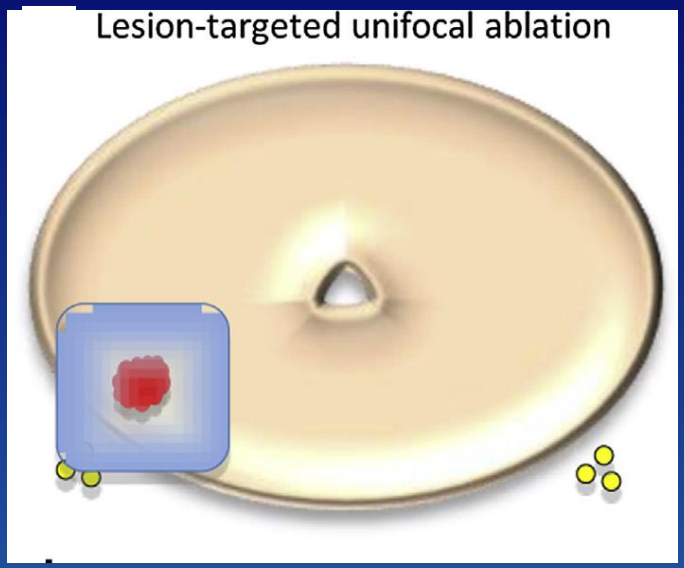
TRUS, mpMRI
TRUS, mpMRI
mpMRI
TRUS
mpMRI

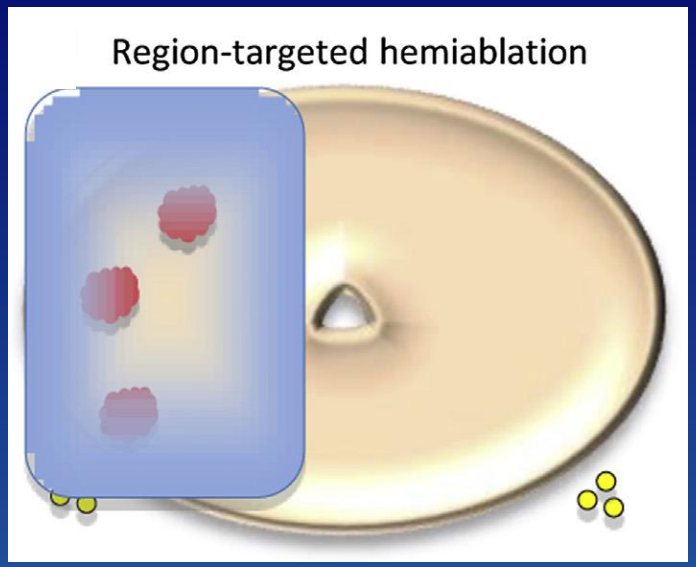






STRATEGIE DI TRATTAMENTO DELLA TERAPIA FOCALE





COME SI VALUTA IL SUCCESSO DI UN TRATTAMENTO ABLATIVO FOCALE?

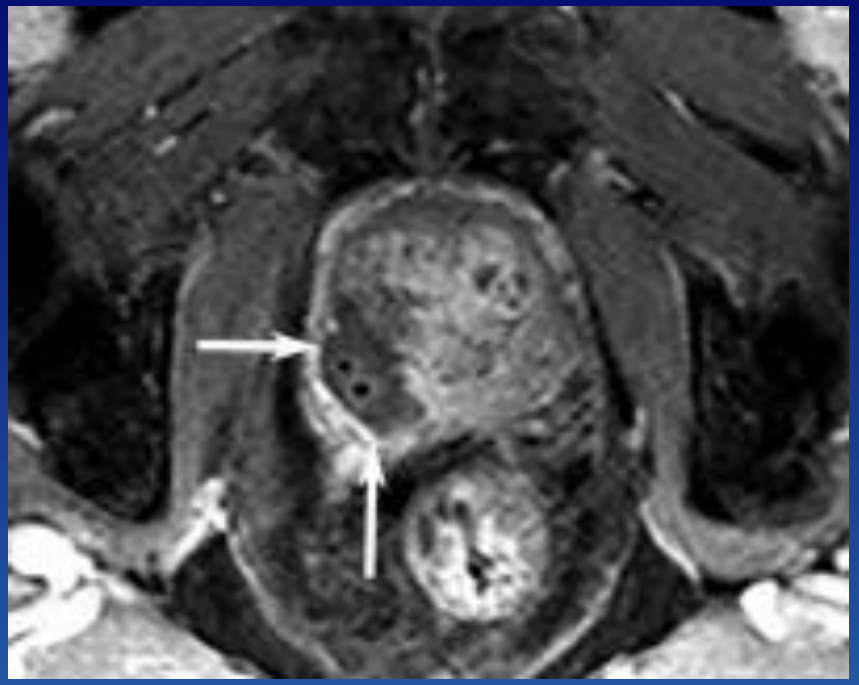
- Negatività alla biopsia di controllo
- Assenza di segni di ricorrenza di malattia all'imaging RM post/ablazione
- Riduzione del PSA ----- PSA nadir

APPROCCIO INTEGRATO

Difficile definire la recidiva di malattia con un singolo parametro

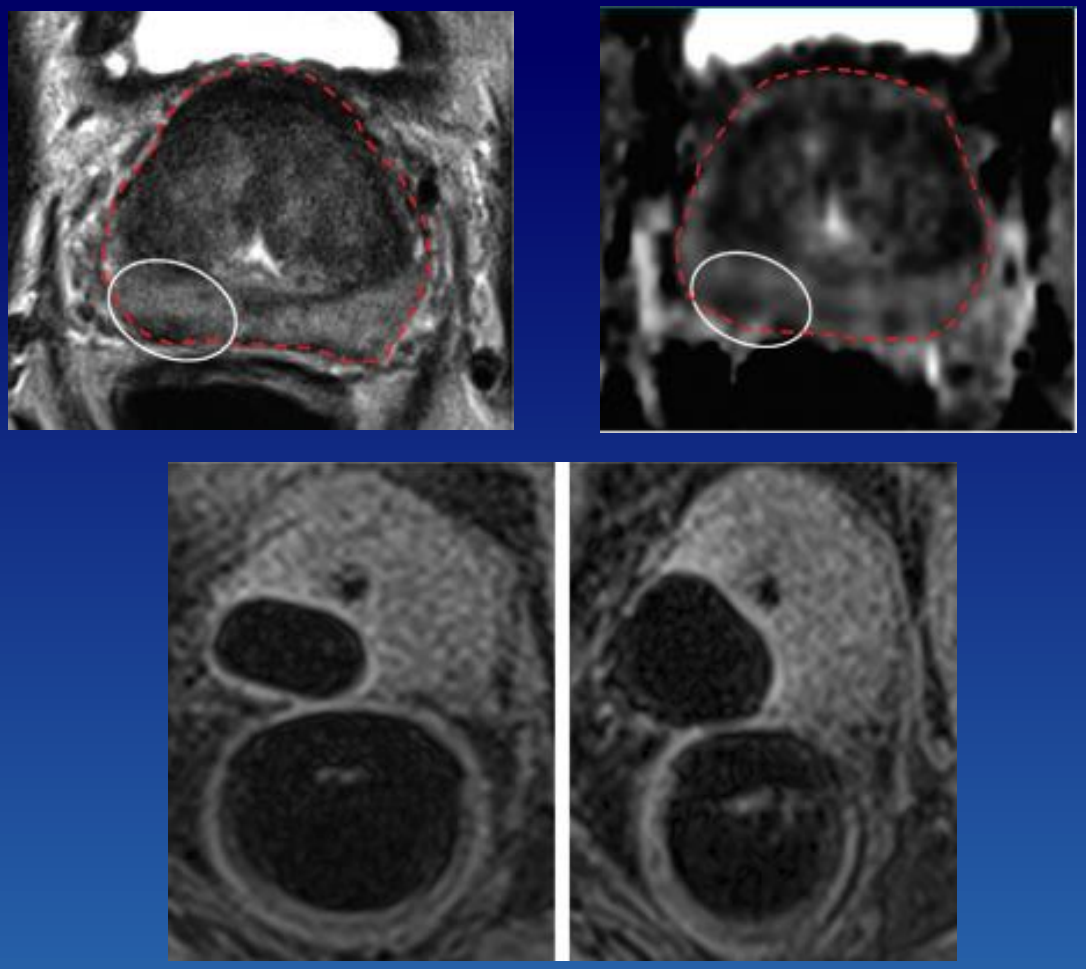
RUOLO DELL'IMAGING RM NELLA TERAPIA FOCALE

- Guida della procedura (FLA)
- Monitoraggio real-time del trattamento
- Valutazione degli effetti immediati-precoci (area di necrosi)
- Disomogenea ed irregolare ipointensità in T2 con alterazione architetturale
- Necessario mdc per la differenziare l'area necrotica dal tessuto vitale - ampia area avascolare



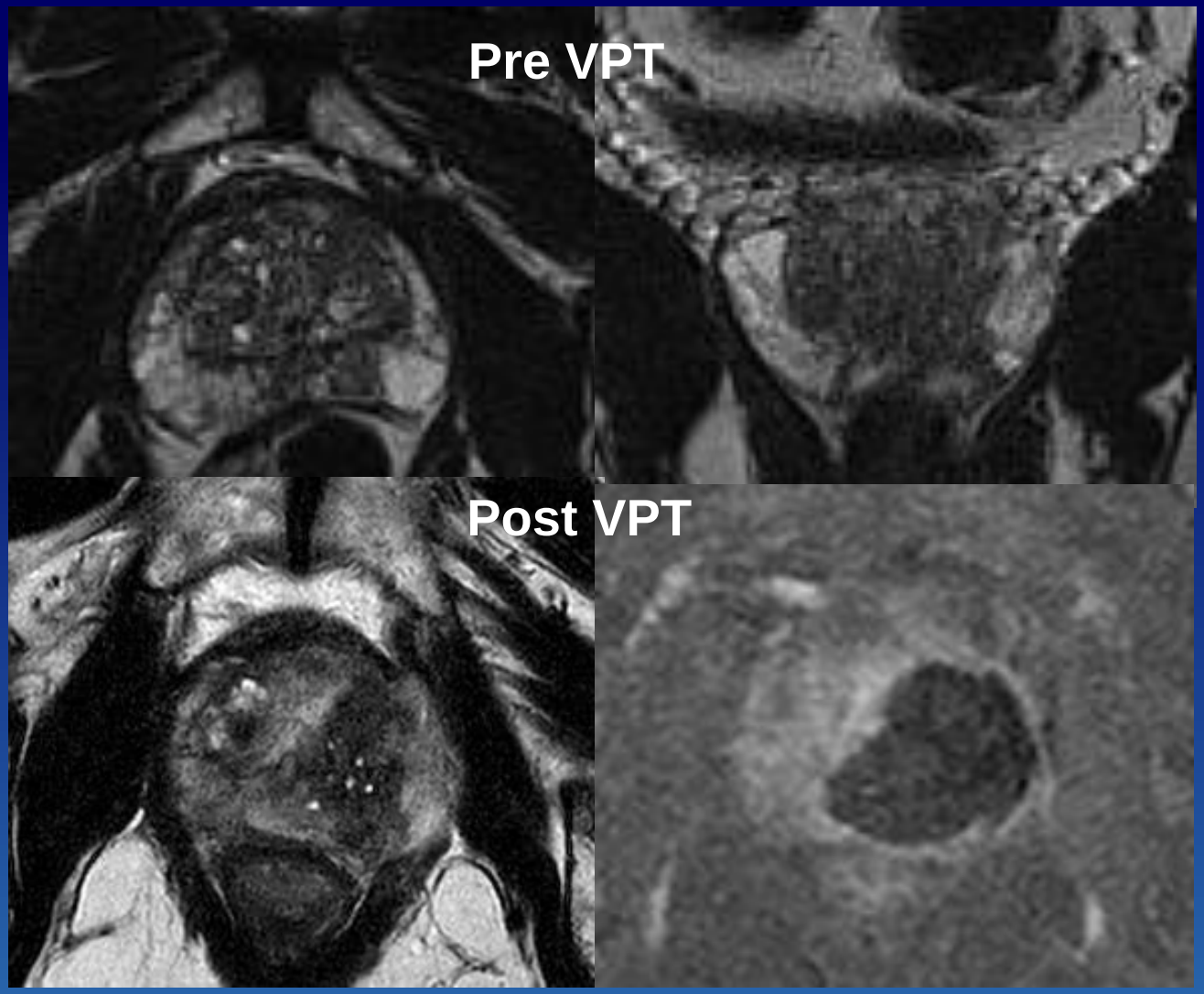
Remember!

RUOLO DELL'IMAGING RM NELLA TERAPIA FOCALE



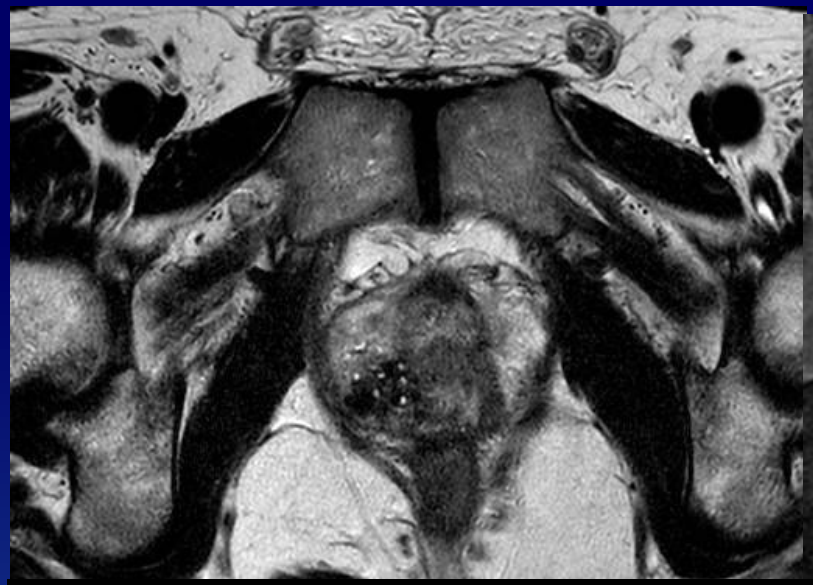
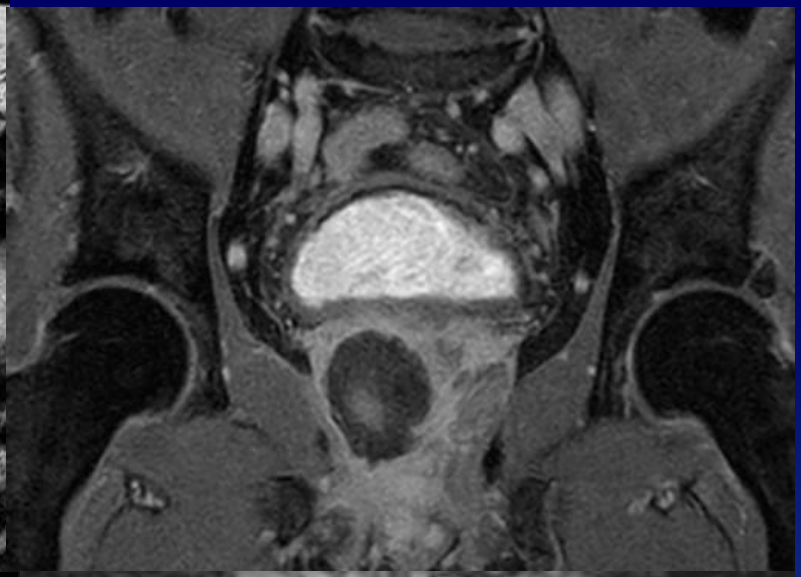
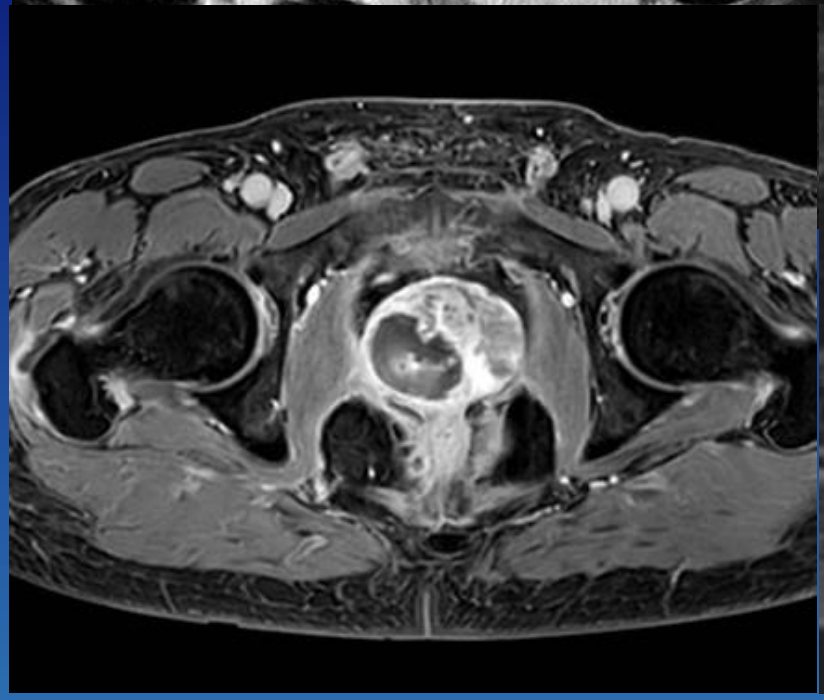
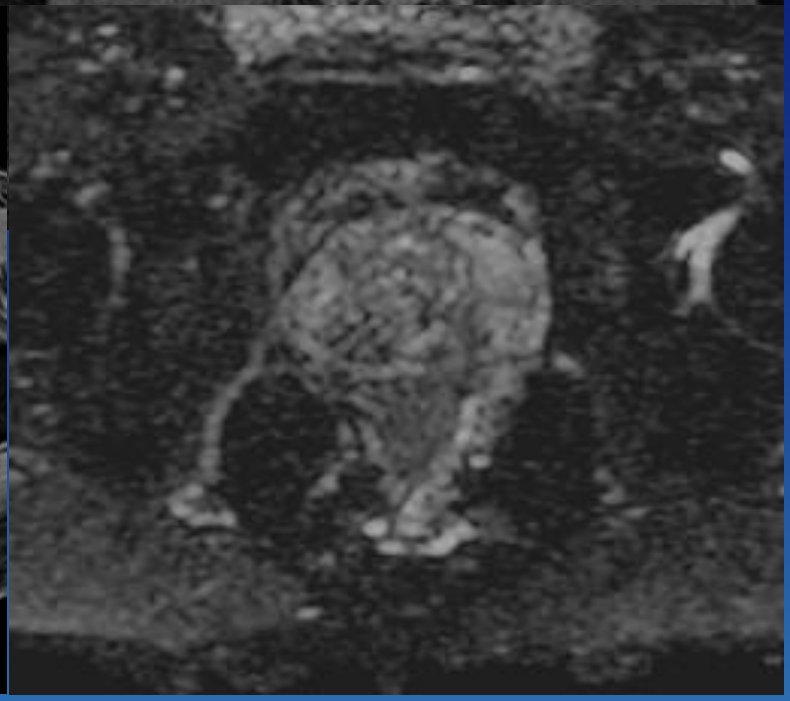
Imaging precoce durante crioterapia

RUOLO DELL'IMAGING RM NELLA TERAPIA FOCALE



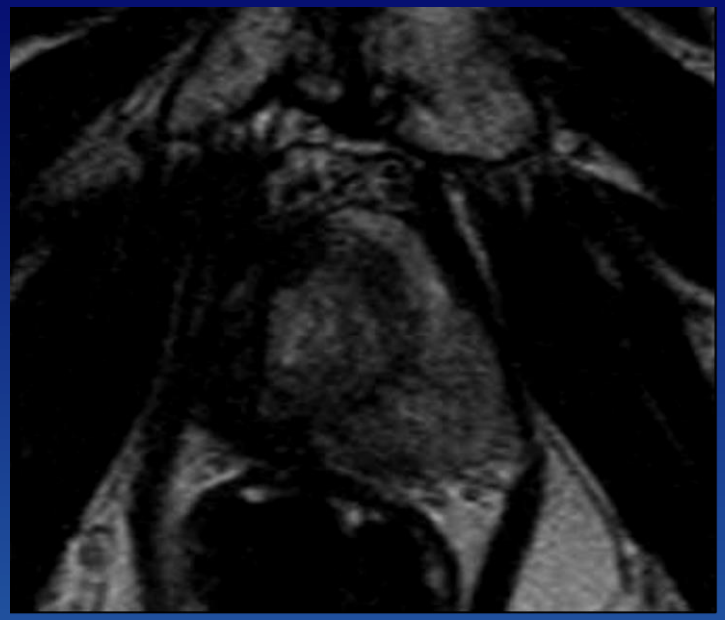
Tookad soluble®
Steba Biotech

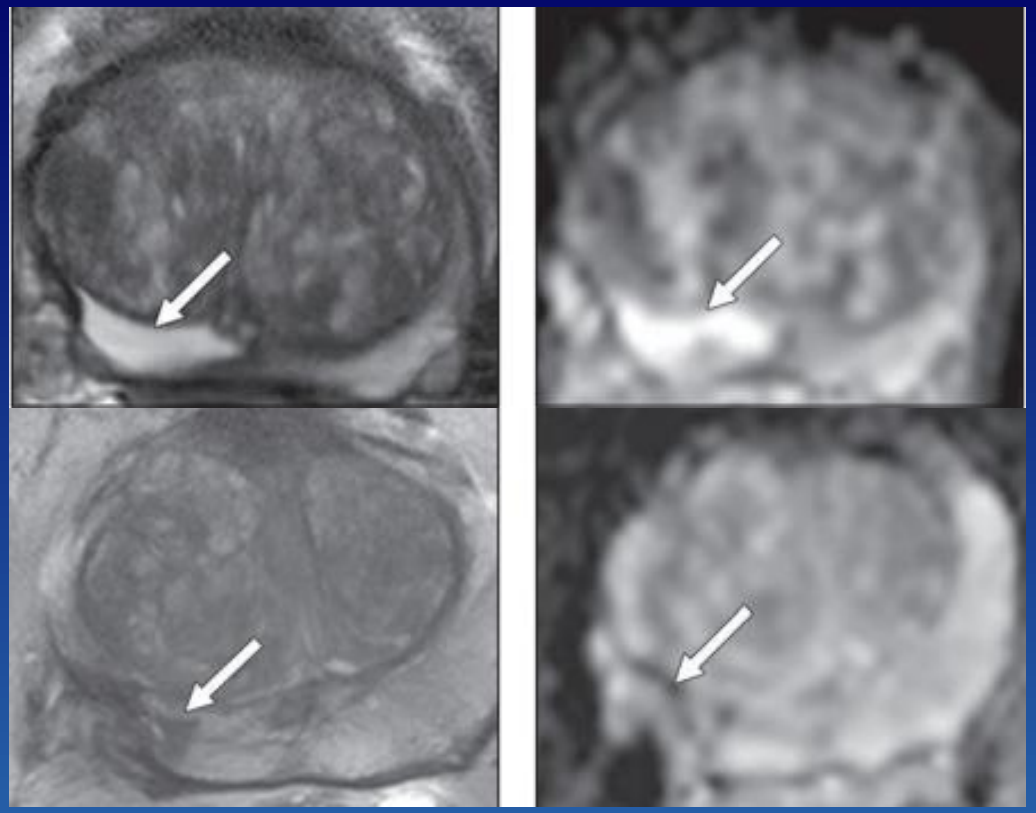
Pz di 64 anni, PSA = 2,58 ng/ml, PHI 40
Biopsie prostatiche: Adenoca GS 6: 2/2 base sx, 2/2 margine laterale sx, 2/2 apice sx, 3/3 PIRADS 4 lobo sx

RUOLO DELL'IMAGING RM NELLA TERAPIA FOCALE

FU terapia focale (effetti a medio-lungo termine, > 12 mesi)





RUOLO DELL'IMAGING RM NELLA TERAPIA FOCALE

Difficile distinzione della **recidiva di malattia** dalla **fibrosi post-trattamento** nelle sequenze **T2 pesate**

NECESSARIE SEQUENZE FUNZIONALI!!!

DCE **(ATTENZIONE RISCHIO DI CONFONDERSI CON LA FLOGOSI POST TRATTAMENTO A < 12 MESI)**

SCARSI DATI SUL FOLLOW-UP A LUNGO TERMINE DOPO TERAPIA FOCALE!

LA TERAPIA FOCALE NEL CARCINOMA DELLA PROSTATA

- TERAPIA EMERGENTE
- SCOPO: RIDURRE EFFETTI COLLATERALI DELLE TERAPIE '*whole gland*'
- PUO' ESSERE PROPOSTA NEI PAZIENTI A BASSO RISCHIO (INTERMEDIO RISCHIO?)
- NON RAPPRESENTA LO STANDARD OF CARE
- DIFFERENTI TECNICHE CON DIVERSI APPROCCI
- APPROCCIO INTEGRATO NEL FOLLOW UP
- RUOLO IMPORTANTE DELL'IMAGING IN FASE PRECOCE E COME GUIDA AL TRATTAMENTO
- NECESSARI ULTERIORI STUDI E TRIAL CLINICI PER L'AFFERMAZIONE COME VERA ALTERNATIVA ALLA SORVEGLIANZA ATTIVA E AL TRATTAMENTO RADICALE
- NECESSARIA CORRETTA SELEZIONE DEI PAZIENTI E STADIAZIONE LOCALE DI MALATTIA

Find the right treatment for the right cancer at the right time!!!!