



Πρόγραμμα 14^{ης} Εκπαιδευτικής Εβδομάδος
Ελλήνων Ειδικευομένων Ουρολόγων
18-22 Φεβρουαρίου 2019
Ξενοδοχείο Athens Marriott

1^η Ημέρα - Δευτέρα 18 Φεβρουαρίου 2019

Καρκίνος του προστάτη και Συμπτώματα από το κατώτερο ουροποιητικό στους άνδρες

09:30 - 11:00 Θεραπεία εντοπισμένης νόσου

09.30-09.50 Ενεργή παρακολούθηση / Ε. Φραγκιάδης

09.50-10.10 Χειρουργική θεραπεία / Μ. Καραβιτάκης

10.10-10.30 Ακτινοβολία / Ε. Μαραγκουδάκης

10.30-10.50 Εστιασμένη θεραπεία / Ι. Βαρκαράκης

10:50-11:00 Ερωτήσεις - συζήτηση

**Δεν υπάρχει
σύγκρουση
συμφερόντων**

ΘΕΜΑΤΑ ΠΡΟΣ ΣΥΖΗΤΗΣΗ

1. 3D-CONFORMAL IMRT V-MAT RADID-ARC IGRT
2. ΣΤΕΡΕΟΤΑΚΤΙΚΗ ΑΚΤΙΝΟΘΕΡΑΠΕΙΑ (SBRT)
3. ΣΥΝΔΙΑΣΜΟΣ ΑΚΤΙΝΟΘΕΡΑΠΕΙΑΣ ΟΡΜΟΝΟΘΕΡΑΠΕΙΑΣ
4. ΠΡΟΣΤΑΤΕΚΤΟΜΗ Ή ΑΚΤΙΝΟΘΕΡΑΠΕΙΑ ΣΕ ΑΣΘΕΝΕΙΣ ΜΕΓΑΛΟΥ ΚΙΝΔΥΝΟΥ
5. ΣΥΜΠΛΗΡΩΜΑΤΙΚΗ ΑΚΤΙΝΟΘΕΡΑΠΕΙΑ ΜΕΤΑ ΑΠΟ ΡΙΖΙΚΗ ΠΡΟΣΤΑΤΕΚΤΟΜΗ
6. ΑΚΤΙΝΟΘΕΡΑΠΕΙΑ ΔΙΑΣΩΣΗΣ ΜΕΤΑ ΑΠΟ ΡΙΖΙΚΗ ΠΡΟΣΤΑΤΕΚΤΟΜΗ
7. ΒΙΟΧΗΜΙΚΗ ΥΠΟΤΡΟΠΗ ΜΕΤΑ ΤΗ ΠΡΟΣΤΑΤΕΚΤΟΜΗ ΚΑΙ ΑΚΤΙΝΟΘΕΡΑΠΕΙΑ

ΑΚΤΙΝΟΘΕΡΑΠΕΙΑ ΣΕ ΑΣΘΕΝΕΙΣ ΜΙΚΡΟΥ ΚΙΝΔΥΝΟΥ

| RISK STRATIFICATION AND STAGING WORKUP | | | | | |
|----------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------|----------------------------------------|
| Risk group | Clinical/pathologic features | Imaging ^{i,j} | Molecular testing of tumor | Germline testing | Initial therapy ^p |
| Very low ^a | <ul style="list-style-type: none"> • T1c AND • Gleason score ≤6/grade group 1 AND • PSA <10 ng/mL AND • Fewer than 3 prostate biopsy fragments/cores positive, ≤50% cancer in each fragment/core AND • PSA density <0.15 ng/mL/g | Not indicated | Not indicated | Consider if strong family history ^c | See PROS-4 |
| Low ^a | <ul style="list-style-type: none"> • T1-T2a AND • Gleason score ≤6/grade group 1 AND • PSA <10 ng/mL | Not indicated | Consider if life expectancy ≥10y ^j | Consider if strong family history ^c | See PROS-5 |
| Favorable intermediate ^a | <ul style="list-style-type: none"> • T2b-T2c OR • Gleason score 3+4=7/grade group 2 OR • PSA 10–20 ng/mL AND • Percentage of positive biopsy cores <50% | <ul style="list-style-type: none"> • Bone imaging^k: not recommended for staging • Pelvic ± abdominal imaging: recommended if nomogram predicts >10% probability of pelvic lymph node involvement | Consider if life expectancy ≥10y ^j | Consider if strong family history ^c | See PROS-6 |
| Unfavorable intermediate ^a | <ul style="list-style-type: none"> • T2b-T2c OR • Gleason score 3+4=7/grade group 2 or Gleason score 4+3=7/grade group 3 OR • PSA 10–20 ng/mL | <ul style="list-style-type: none"> • Bone imaging^k: recommended if T2 and PSA >10 ng/mL • Pelvic ± abdominal imaging: recommended if nomogram predicts >10% probability of pelvic lymph node involvement | Not routinely recommended | Consider if strong family history ^c | See PROS-7 |
| High | <ul style="list-style-type: none"> • T3a OR • Gleason score 8/grade group 4 or Gleason score 4+5=9/grade group 5 OR • PSA >20 ng/mL | <ul style="list-style-type: none"> • Bone imaging^k: recommended • Pelvic ± abdominal imaging: recommended if nomogram predicts >10% probability of pelvic lymph node involvement | Not routinely recommended | Consider ^o | See PROS-8^p |
| Very high | <ul style="list-style-type: none"> • T3b-T4 OR • Primary Gleason pattern 5 OR • >4 cores with Gleason score 8–10/ grade group 4 or 5 | <ul style="list-style-type: none"> • Bone imaging^k: recommended • Pelvic ± abdominal imaging: recommended if nomogram predicts >10% probability of pelvic lymph node involvement | Not routinely recommended | Consider ^o | See PROS-8^p |
| Regional | Any T, N1, M0 | Already performed | Consider tumor testing for homologous recombination gene mutations and for microsatellite instability (MSI) or mismatch repair deficiency (dMMR) ^{m,n} | Consider ^o | See PROS-9 |
| Metastatic | Any T, Any N, M1 | Already performed | Consider tumor testing for homologous recombination gene mutations and for MSI or dMMR ^{m,n} | Consider ^o | See PROS-13 |

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

8. Clinicians **should** recommend active surveillance as the preferable care option for most **low risk** localized prostate cancer patients. (Moderate Recommendation; Evidence Level: Grade B)
9. Clinicians **may offer** definitive treatment (i.e. radical prostatectomy or radiotherapy) to select **low risk** localized prostate cancer patients who may have a high probability of progression on active surveillance. (Conditional Recommendation; Evidence Level: Grade B)
10. Clinicians **should not add androgen deprivation therapy (ADT) along with radiotherapy for low risk** localized prostate cancer with the exception of reducing the size of the prostate for brachytherapy. (Strong Recommendation; Evidence Level: Grade B)

Clinically Localized Prostate Cancer: AUA/ASTRO/SUO Guideline. Part II: Recommended Approaches and Details of Specific Care Options Martin G. Sanda et al.

48. Clinicians should inform localized prostate cancer patients who are **considering proton beam therapy that it offers no clinical advantage over other forms of definitive treatment.** (Moderate Recommendation; Evidence Level: Grade C)

49. Clinicians should inform localized prostate cancer patients considering **brachytherapy that it has similar effects as EBRT with regard to erectile dysfunction and proctitis but can also exacerbate urinary obstructive symptoms.** (Expert Opinion)

Clinically Localized Prostate Cancer: AUA/ASTRO/SUO Guideline.

Part II: Recommended Approaches and Details of Specific Care Options

Martin G. Sanda et al.

42. Clinicians may offer single modality EBRT or brachytherapy for patients who elect radiotherapy for **low risk** localized prostate cancer. (Clinical Principle)
45. Clinicians should inform localized prostate cancer patients that use of **ADT with radiation increases the likelihood and severity of **adverse treatment-related**** events on sexual function in most men and can cause other systemic side effects. (Strong Recommendation; Evidence Level: Grade B)
43. Clinicians may offer EBRT or brachytherapy alone or in combination for **favorable intermediate risk** localized prostate cancer. (Clinical Principle)
44. Clinicians should offer 24-36 months of ADT as an adjunct to either EBRT alone or EBRT combined with brachytherapy to patients electing radiotherapy for **high risk** localized prostate cancer. (Strong Recommendation; Evidence Level: Grade A)

ΑΚΤΙΝΟΘΕΡΑΠΕΙΑ ΣΕ ΑΣΘΕΝΕΙΣ ΜΙΚΡΟΥ ΚΙΝΔΥΝΟΥ

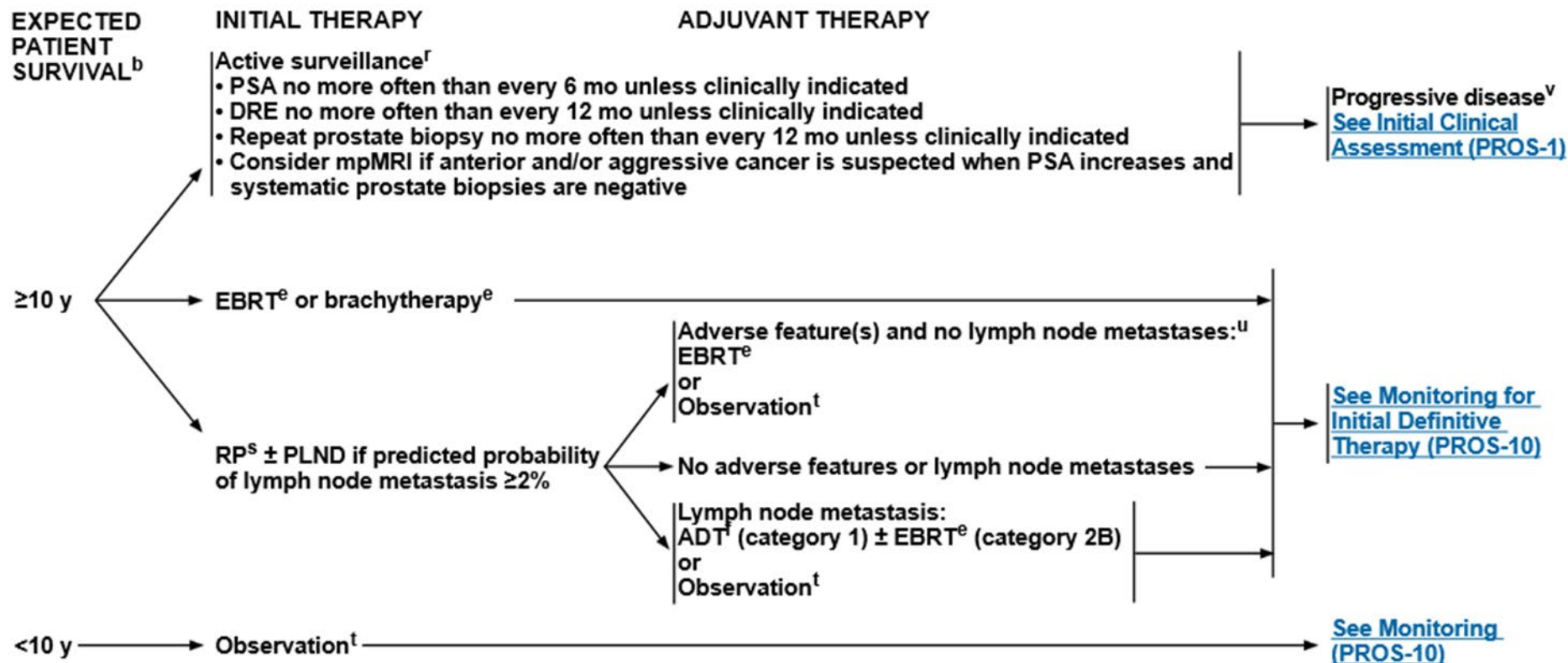
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NCCN Guidelines Version 2.2018 Prostate Cancer

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LOW RISK GROUP



ΑΚΤΙΝΟΘΕΡΑΠΕΙΑ ΣΕ ΑΣΘΕΝΕΙΣ ΜΙΚΡΟΥ ΚΙΝΔΥΝΟΥ

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PRINCIPLES OF RADIATION THERAPY

Table 1: Regimens that have shown acceptable efficacy and toxicity. The optimal regimen for an individual patient warrants evaluation of comorbid conditions, voiding symptoms, and toxicity of therapy. Additional fractionation schemes may be used as long as sound oncologic principles and appropriate estimate of BED are considered.

| Regimen for Definitive Therapy | NCCN Risk Group (* indicates an appropriate regimen option if radiation therapy is given) | | | | | |
|---------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------|------------------|--------------------------------------------------------|-------------------------------------------------------------|---------------------------------|------------------|
| | Very-Low ¹ | Low ¹ | Favorable or good prognostic ² intermediate | Unfavorable, or poor prognostic ² , intermediate | High and Very-High ³ | Node Positive |
| Beam Therapies | | | | | | |
| 72 Gy to 80 Gy at 2 Gy per fraction | ✓ | ✓ | ✓ | ✓ with 4-6 mo ADT | ✓ with 2-3 y ADT | ✓ with 2-3 y ADT |
| 75.8 Gy to 81.0 Gy at 1.8 Gy per fraction | ✓ | ✓ | ✓ | ✓ with 4-6 mo ADT | ✓ with 2-3 y ADT | ✓ with 2-3 y ADT |
| 70.2 Gy at 2.7 Gy per fraction | ✓ | ✓ | ✓ | ✓ with 4-6 mo ADT | ✓ with 2-3 y ADT | ✓ with 2-3 y ADT |
| 70 Gy at 2.5 Gy per fraction | ✓ | ✓ | ✓ | ✓ with 4-6 mo ADT | ✓ with 2-3 y ADT | ✓ with 2-3 y ADT |
| 60 Gy at 3 Gy per fraction | ✓ | ✓ | ✓ | ✓ with 4-6 mo ADT | ✓ with 2-3 y ADT | ✓ with 2-3 y ADT |
| 51.8 Gy at 4.3 Gy per fraction | ✓ | ✓ | ✓ | | | |
| 37 Gy at 7.4 Gy per fraction | ✓ | ✓ | ✓ | | | |
| 40 Gy at 8 Gy per fraction | ✓ | ✓ | ✓ | | | |
| 38.25 Gy at 7.25 Gy per fraction | ✓ | ✓ | ✓ | | | |
| Brachytherapy Monotherapy | | | | | | |
| Iodine 125 implant at 145 Gy | ✓ | ✓ | ✓ | | | |
| Palladium 103 implant at 125 Gy | ✓ | ✓ | ✓ | | | |
| Cesium implant at 115 Gy | ✓ | ✓ | ✓ | | | |
| HDR 27 Gy at 13.5 Gy in 2 implants | ✓ | ✓ | ✓ | | | |
| HDR 38 Gy at 9.5 Gy BID in 2 implants | ✓ | ✓ | ✓ | | | |
| Combined EBRT and Brachytherapy (EBRT 45–50.4 Gy at 1.8–2.0 Gy/fx, unless otherwise noted) | | | | | | |
| Iodine 125 implant at 110–115 Gy | | | | ✓ ± 4 mo ADT | ✓ with 1-3 y ADT | ✓ with 1-3 y ADT |
| Palladium 103 implant at 90–100 Gy | | | | ✓ ± 4 mo ADT | ✓ with 1-3 y ADT | ✓ with 1-3 y ADT |
| Cesium implant at 85 Gy | | | | ✓ ± 4 mo ADT | ✓ with 1-3 y ADT | ✓ with 1-3 y ADT |
| HDR 21.5 Gy at 10.75 Gy x 2 | | | | ✓ ± 4 mo ADT | ✓ with 1-3 y ADT | ✓ with 1-3 y ADT |
| EBRT 37.5 Gy at 2.5 Gy + 12–15 Gy single HDR | | | | ✓ ± 4 mo ADT | ✓ with 1-3 y ADT | ✓ with 1-3 y ADT |

¹Active surveillance should be strongly considered

²“Good” or “Poor” prognostic is not strictly defined. Predictive nomograms and/or molecular testing can be used to prognosticate PSA persistence/recurrence, prostate cancer specific mortality and metastasis free survival after definitive external beam radiation therapy. Although the prognostic value has been established, the predictive value of these tests remains unknown.

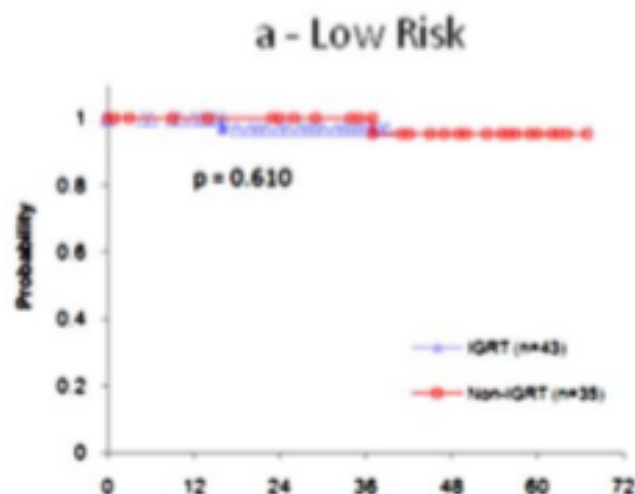
³Prophylactic nodal radiation may be considered if estimate of nodal metastasis is high.

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

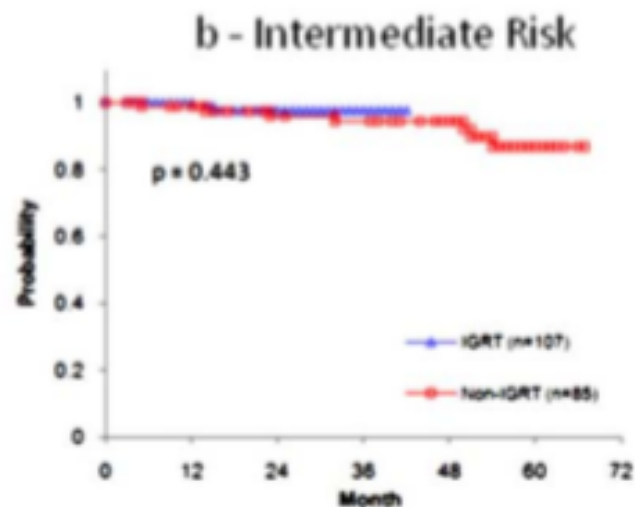
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EBRT: Improving Outcomes IMAGE GUIDANCE

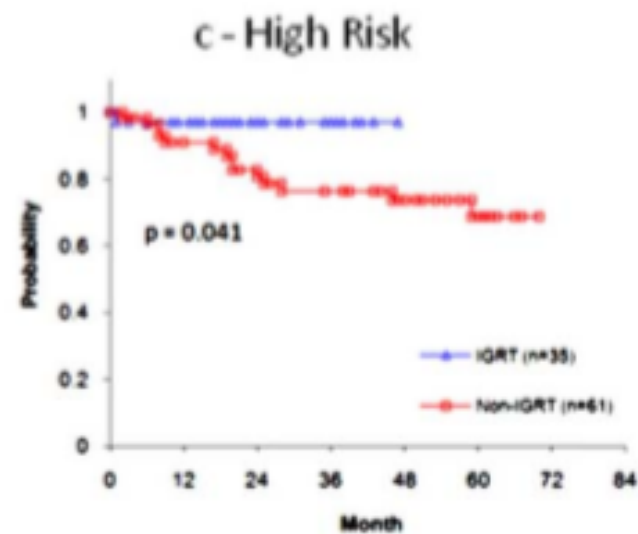


Number of subjects at risk

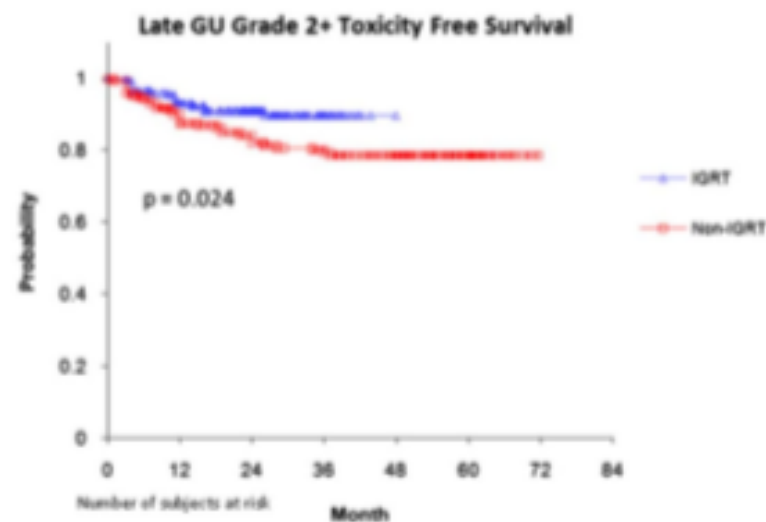
| Month | 0 | 12 | 24 | 36 | 48 | 60 | 72 |
|----------|----|----|----|----|----|----|----|
| IGRT | 43 | 38 | 24 | 6 | | | |
| Non-IGRT | 36 | 31 | 29 | 23 | 17 | 7 | |



| Month | 0 | 12 | 24 | 36 | 48 | 60 | 72 |
|----------|-----|----|----|----|----|----|----|
| IGRT | 108 | 93 | 54 | 9 | | | |
| Non-IGRT | 87 | 78 | 67 | 65 | 50 | 18 | |



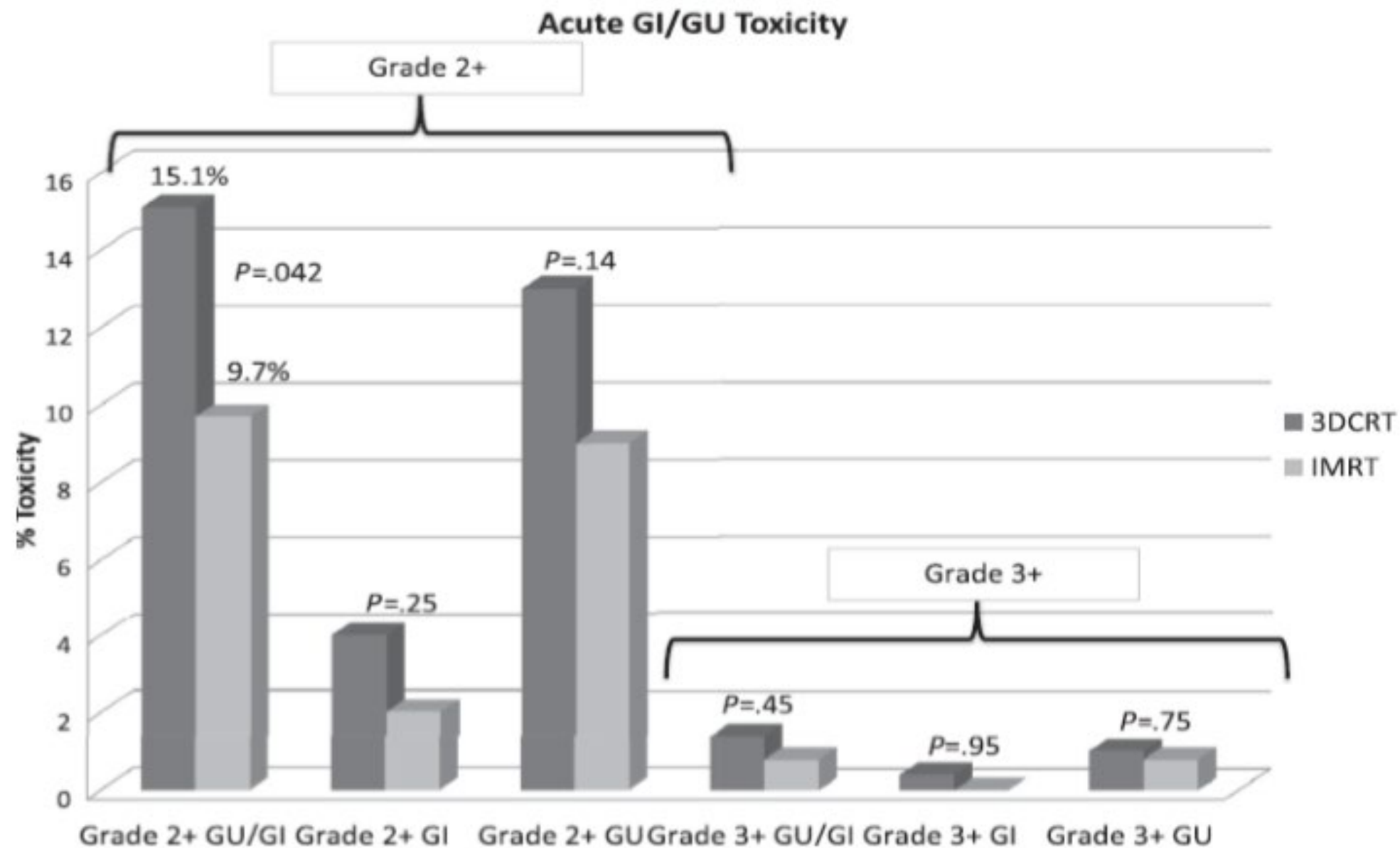
| Month | 0 | 12 | 24 | 36 | 48 | 60 | 72 | 84 |
|----------|----|----|----|----|----|----|----|----|
| IGRT | 35 | 28 | 18 | 9 | | | | |
| Non-IGRT | 67 | 49 | 42 | 35 | 27 | 14 | | |



MSKCC: STARTED IGRT IN 2007
Less biochemical failures
Less toxicity (GU)

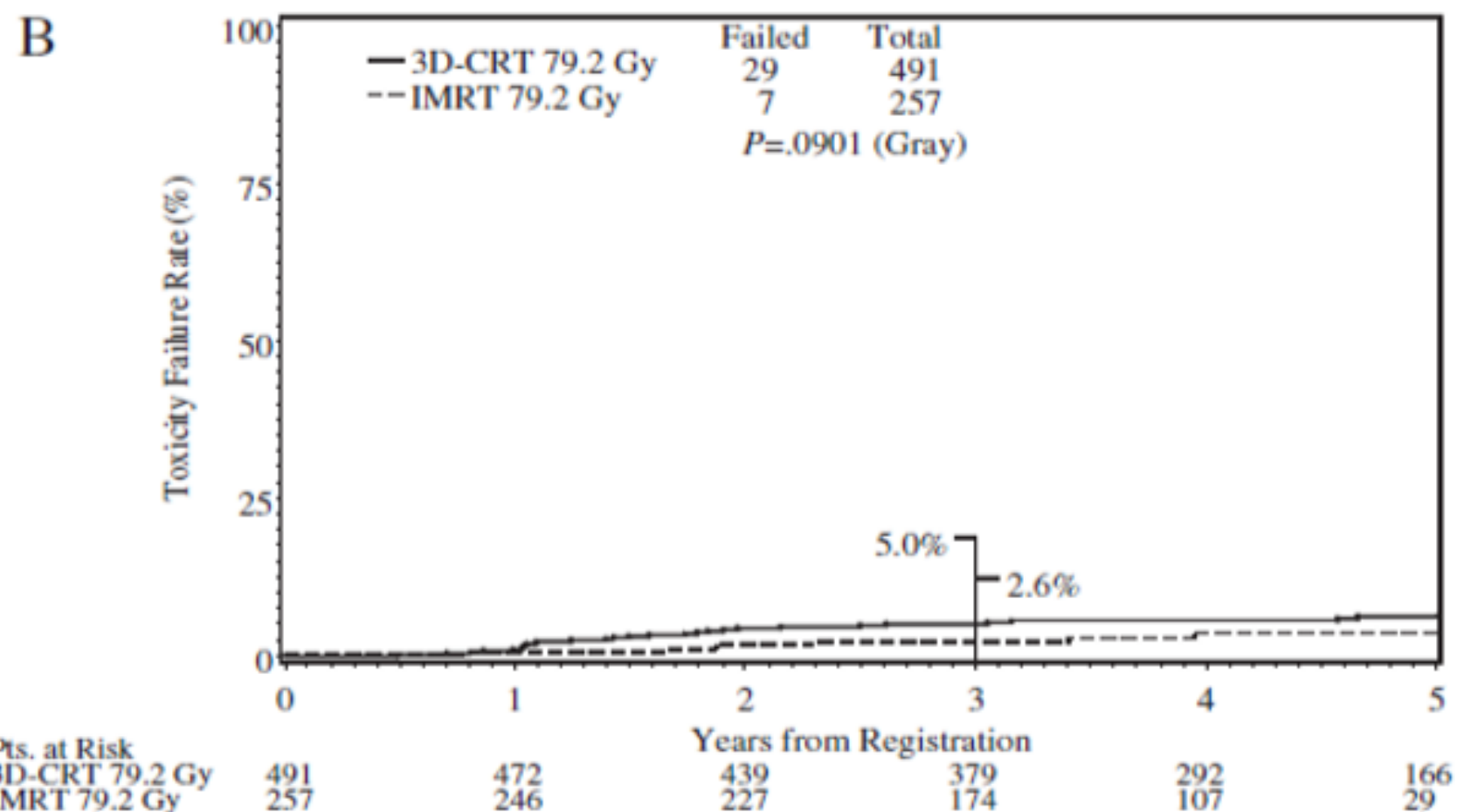
Zelevsky, IJROBP, 84, 125-129, 2012

IMRT vs 3DRT: RTOG 0126 - Acute Toxicity



IMRT vs 3DRT: RTOG 0126 - Late GI Toxicity

Late Grade 3+ GI Toxicity



RT DOSE: Randomized Trials

MDACC Trial (Pollack):

70 vs 78 Gy

bNED

50 vs 73%

at 10 years

p<0.01

MGH/LLUMC (Proton Trial):

70 vs 79.2 Gy

Low risk

72 vs 93%

at 10 years

p<0.01

Int risk

58 vs 70%

p=0.06

Dutch Multi-institutional Trial:

68 vs 78 Gy (some ADT)

45 vs 56%

at 7 years

p=0.03

UK (MRC) Trial:

64 vs 74 Gy (some ADT)

71 vs 60%

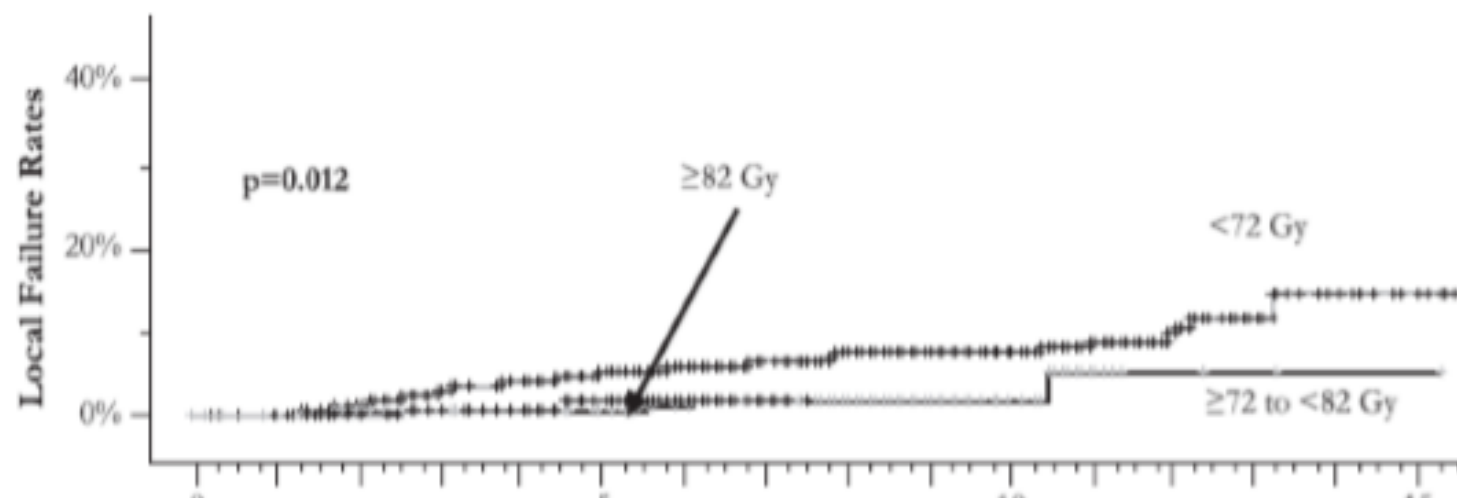
at 5 years

p<0.01

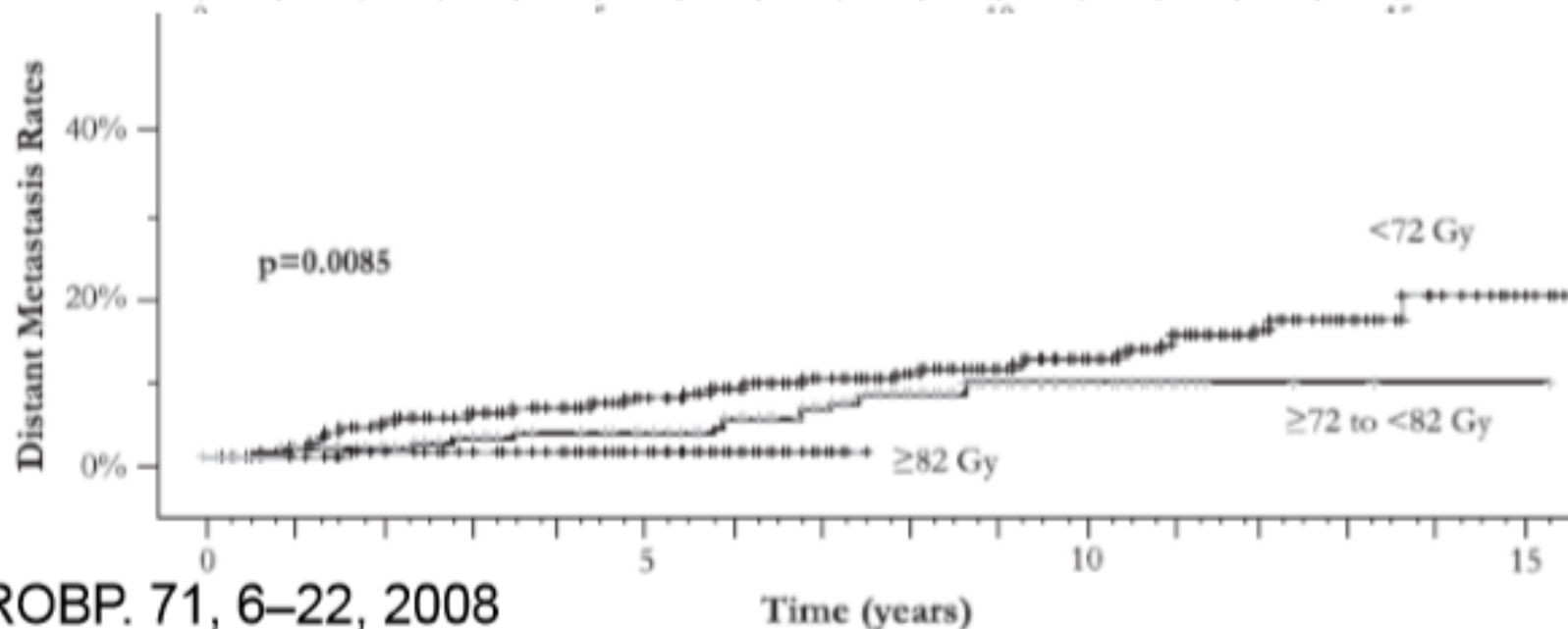
IMPACT OF INCREASED DOSE

919 Stage T1-T3N0M0 - RT alone - treated between 1986 and 2000

LOCAL
FAILURE



DISTANT
FAILURE



LOCALIZED PROSTATE CA: RT DOSE



Int. J. Radiation Oncology Biol. Phys., Vol. 46, No. 3, pp. 567-574, 2000
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0360-3016/00/\$-see front matter

PII S0360-3016(99)00455-1

CLINICAL INVESTIGATION

Prostate

HIGHER THAN STANDARD RADIATION DOSES (≥ 72 Gy) WITH OR WITHOUT ANDROGEN DEPRIVATION IN THE TREATMENT OF LOCALIZED PROSTATE CANCER

PATRICK A. KUPELIAN, M.D.,* DASARAHALLY S. MOHAN, M.D.,* JANICE LYONS, M.D.,*
ERIC A. KLEIN, M.D.,[†] AND CHANDANA A. REDDY, M.S.*

Departments of *Radiation Oncology and [†]Urology, Cleveland Clinic Foundation, Cleveland, OH

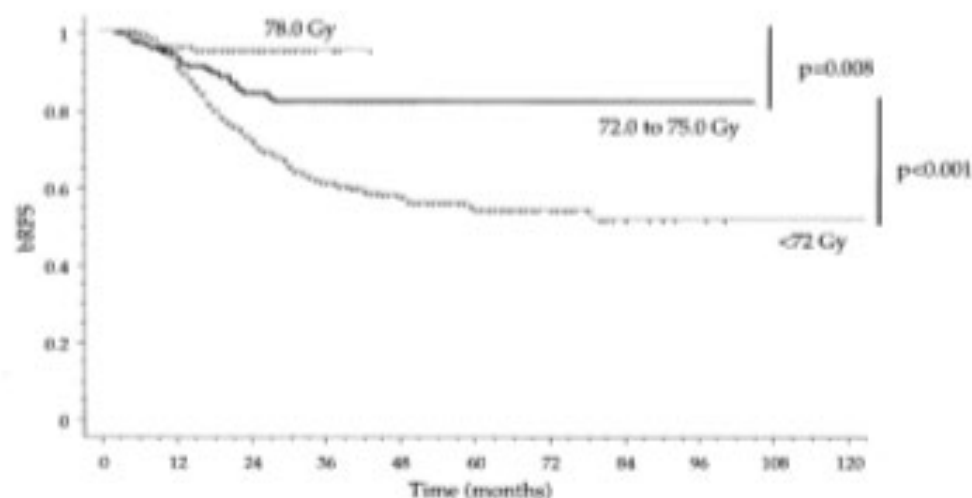


Fig. 4. bRFS by radiation dose grouped in three dose levels; <72 Gy, 72.0 to 75.0 Gy, and 78.0 Gy. Symbols represent censored events.

Need Better Local Therapy: Doses >80 Gy?

Prostate Biopsy: Local Failure Endpoint

Zelevsky et al., MSKCC

1989-1998: 220 RT patients biopsied at 3 years.

3 mos AD: 29% Median RT dose: 76 Gy (range: 65-81 Gy)

| Positive biopsies | | | | Positive biopsies | | |
|-------------------|---------|-----|-----------|-------------------|-----|-----------|
| RT Dose | 64.8 Gy | 52% | p < 0.001 | No ADT | 34% | p < 0.001 |
| | 70.2 Gy | 34% | | ADT | 11% | |
| | 75.6 Gy | 24% | | | | |
| | 81 Gy | 9% | | | | |

NO IMAGE GUIDANCE:

GEOGRAPHIC MISS versus INSUFFICIENT DOSE?



SBRT for Prostate Cancer

Patrick Kupelian, M.D.
Professor and Vice Chair
University of California Los Angeles
Department of Radiation Oncology
pkupelian@mednet.ucla.edu

June 2014

Planning

PTV: 95% of PTV volume to get 95-110% of Rx dose.

SBRT: (8 Gy x 5)

OAR Dose Constraints:

Rectum V50 (20 Gy) \leq 50%

V80 (32 Gy) \leq 20%

V90 (36 Gy) \leq 10%

V100 (40 Gy) \leq 5%

Bladder V50 (20 Gy) \leq 40%

V100 (40 Gy) \leq 1.1%

Femurs V40 (16 Gy) \leq 5%

Small Bowel V50 (20 Gy) $<$ 1%

Delivery

Efficacy of SBRT

Multi-institutional pooled data; 8 institutions

1100 patients, ~ 3 yr median FU (6-72 mos)

335 cases with a >4 years follow-up (median 53 mos)

35-40 Gy in 4-5 fractions, ADT in 14%

Risk groups:

Low: 639 59%

Intermediate: 326 30%

High: 124 11%

**King et al,
Radiother Oncol.
109:217-21, 2013**

Subset with longer follow-up:

335 cases with >4 years follow-up
(median: 53 months)

5-year bRFS rates:

Low risk: 97%

Intermediate-risk: 89%

UT Southwestern Protocol (R. Timmerman)

ASTRO 2013 Update. Abstract 2405

Median follow-up is 25.5 months

Dose groups: 9.0 Gy x 5 = 45 Gy
 9.5 Gy x 5 = 47.5 Gy
 10.0 Gy x 5 = 50 Gy

10% developed High Grade Rectal Toxicity (Grade 4)

Predictors of Gr4 rectal toxicity

- Diabetes (trend $p=0.06$)
- > 35% of rectal wall ≥ 50 Gy ($p=0.03$)
- Volume of rectal wall receiving 50 Gy ($p=0.01$)

Gr4 patients had $> 3.5 \text{ cm}^3$ of rectal wall ≥ 50 Gy ($p < .0001$).

Patients with no rectal toxicity had $< 3.5 \text{ cm}^3$ rectal wall at 50 Gy.

DO NOT treat with 50 Gy at 10 Gy per fraction

SBRT for Prostate Cancer May Result in More Complications

• [Anna Azvolinsky](#), Mar 17, 2014, [Prostate Cancer](#), [Genitourinary Cancers](#), [Radiation Oncology](#)

Six months following treatment, **15.6% of patients treated with SBRT had a genitourinary toxicity compared with 12.6% of those treated with IMRT** (odds ratio [OR] = 1.29; ***P* = .009**).

At 24 months after treatment initiation, patients treated with SBRT had increased side effects, including **urethritis, urinary incontinence, and obstruction**.

Of patients treated **with SBRT, 43.9% had a genitourinary toxicity compared with 36.3% of those treated with IMRT (OR = 1.38; *P* = .001)**.

The incidence of a fistula is a concern with SBRT, but the current study found no significant differences in the incidence using either technique.

The average per-patient cost of SBRT was \$13,645 compared with \$21,023 for IMRT.

SBRT is still preferable to IMRT for **both patients and insurers**, as SBRT is more convenient and of shorter treatment duration, is less expensive overall compared with IMRT

ΑΚΤΙΝΟΘΕΡΑΠΕΙΑ ΣΕ ΑΣΘΕΝΕΙΣ ΜΕΓΑΛΟΥ ΚΙΝΔΥΝΟΥ

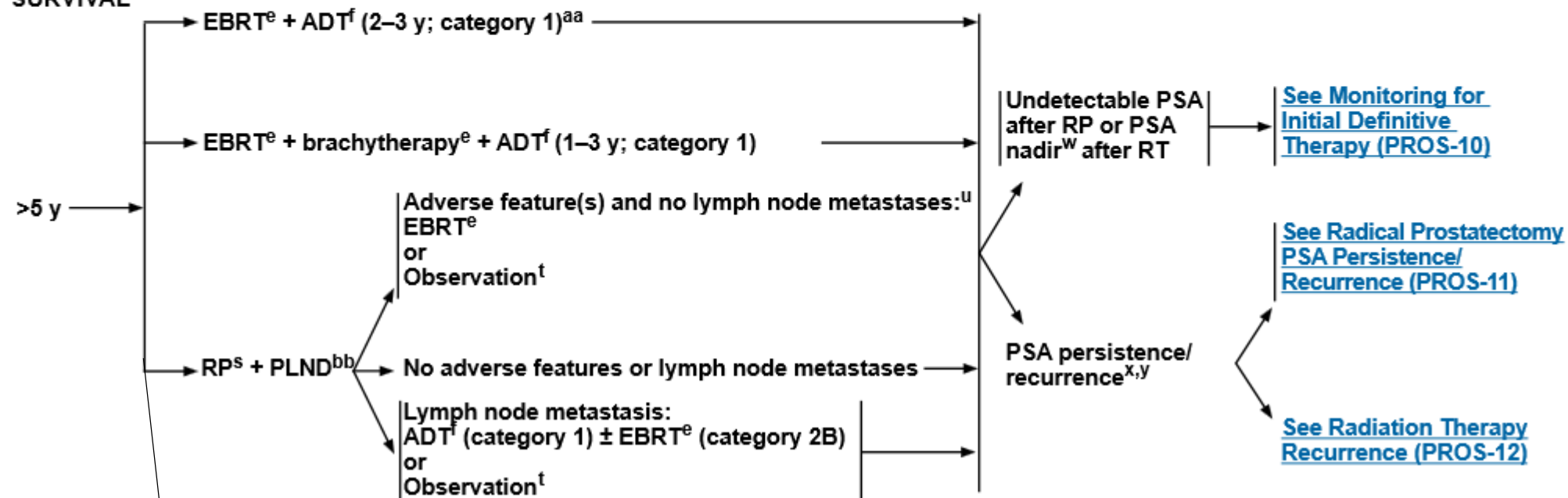
| RISK STRATIFICATION AND STAGING WORKUP | | | | | |
|----------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------|----------------------------------------|
| Risk group | Clinical/pathologic features | Imaging ^{i,j} | Molecular testing of tumor | Germline testing | Initial therapy ^p |
| Very low ^g | <ul style="list-style-type: none"> • T1c AND • Gleason score ≤6/grade group 1 AND • PSA <10 ng/mL AND • Fewer than 3 prostate biopsy fragments/cores positive, ≤50% cancer in each fragment/core AND • PSA density <0.15 ng/mL/g | Not indicated | Not indicated | Consider if strong family history ^c | See PROS-4 |
| Low ^g | <ul style="list-style-type: none"> • T1-T2a AND • Gleason score ≤6/grade group 1 AND • PSA <10 ng/mL | Not indicated | Consider if life expectancy ≥10y ^l | Consider if strong family history ^c | See PROS-5 |
| Favorable intermediate ^g | <ul style="list-style-type: none"> • T2b-T2c OR • Gleason score 3+4=7/grade group 2 OR • PSA 10–20 ng/mL AND • Percentage of positive biopsy cores <50% | <ul style="list-style-type: none"> • Bone imaging^k: not recommended for staging • Pelvic ± abdominal imaging: recommended if nomogram predicts >10% probability of pelvic lymph node involvement | Consider if life expectancy ≥10y ^l | Consider if strong family history ^c | See PROS-6 |
| Unfavorable intermediate ^g | <ul style="list-style-type: none"> • T2b-T2c OR • Gleason score 3+4=7/grade group 2 or Gleason score 4+3=7/grade group 3 OR • PSA 10–20 ng/mL | <ul style="list-style-type: none"> • Bone imaging^k: recommended if T2 and PSA >10 ng/mL • Pelvic ± abdominal imaging: recommended if nomogram predicts >10% probability of pelvic lymph node involvement | Not routinely recommended | Consider if strong family history ^c | See PROS-7 |
| High | <ul style="list-style-type: none"> • T3a OR • Gleason score 8/grade group 4 or Gleason score 4+5=9/grade group 5 OR • PSA >20 ng/mL | <ul style="list-style-type: none"> • Bone imaging^k: recommended • Pelvic ± abdominal imaging: recommended if nomogram predicts >10% probability of pelvic lymph node involvement | Not routinely recommended | Consider ^o | See PROS-8^p |
| Very high | <ul style="list-style-type: none"> • T3b-T4 OR • Primary Gleason pattern 5 OR • >4 cores with Gleason score 8–10/ grade group 4 or 5 | <ul style="list-style-type: none"> • Bone imaging^k: recommended • Pelvic ± abdominal imaging: recommended if nomogram predicts >10% probability of pelvic lymph node involvement | Not routinely recommended | Consider ^o | See PROS-8^p |
| Regional | Any T, N1, M0 | Already performed | Consider tumor testing for homologous recombination gene mutations and for microsatellite instability (MSI) or mismatch repair deficiency (dMMR) ^{m,n} | Consider ^o | See PROS-9 |
| Metastatic | Any T, Any N, M1 | Already performed | Consider tumor testing for homologous recombination gene mutations and for MSI or dMMR ^{m,n} | Consider ^o | See PROS-13 |

HIGH OR VERY HIGH RISK GROUP

**EXPECTED
PATIENT
SURVIVAL^b**

INITIAL THERAPY

ADJUVANT THERAPY



- High Risk
 - ▶ Prophylactic nodal radiation can be considered. ADT is required unless medically contraindicated. The duration of ADT may be reduced when EBRT is combined with brachytherapy. Brachytherapy combined with ADT (without EBRT), or SBRT combined with ADT, can be considered when delivering longer courses of EBRT would present a medical or social hardship.
- Very High Risk
 - ▶ Prophylactic nodal radiation should be considered. ADT is required unless medically contraindicated.

ΑΚΤΙΝΟΘΕΡΑΠΕΙΑ ΣΕ ΑΣΘΕΝΕΙΣ ΜΕΓΑΛΟΥ ΚΙΝΔΥΝΟΥ

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PRINCIPLES OF RADIATION THERAPY

Table 1: Regimens that have shown acceptable efficacy and toxicity. The optimal regimen for an individual patient warrants evaluation of comorbid conditions, voiding symptoms, and toxicity of therapy. Additional fractionation schemes may be used as long as sound oncologic principles and appropriate estimate of BED are considered.

| Regimen for Definitive Therapy | NCCN Risk Group (✓ indicates an appropriate regimen option if radiation therapy is given) | | | | | Node Positive |
|---------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------|------------------|--------------------------------------------------------|-------------------------------------------------------------|---------------------------------|------------------|
| | Very-Low ¹ | Low ¹ | Favorable or good prognostic ² intermediate | Unfavorable, or poor prognostic ² , intermediate | High and Very-High ³ | |
| Beam Therapies | | | | | | |
| 72 Gy to 80 Gy at 2 Gy per fraction | ✓ | ✓ | ✓ | ✓ with 4-6 mo ADT | ✓ with 2-3 y ADT | ✓ with 2-3 y ADT |
| 75.6 Gy to 81.0 Gy at 1.8 Gy per fraction | ✓ | ✓ | ✓ | ✓ with 4-6 mo ADT | ✓ with 2-3 y ADT | ✓ with 2-3 y ADT |
| 70.2 Gy at 2.7 Gy per fraction | ✓ | ✓ | ✓ | ✓ with 4-6 mo ADT | ✓ with 2-3 y ADT | ✓ with 2-3 y ADT |
| 70 Gy at 2.5 Gy per fraction | ✓ | ✓ | ✓ | ✓ with 4-6 mo ADT | ✓ with 2-3 y ADT | ✓ with 2-3 y ADT |
| 80 Gy at 3 Gy per fraction | ✓ | ✓ | ✓ | ✓ with 4-6 mo ADT | ✓ with 2-3 y ADT | ✓ with 2-3 y ADT |
| 51.6 Gy at 4.3 Gy per fraction | ✓ | ✓ | ✓ | | | |
| 37 Gy at 7.4 Gy per fraction | ✓ | ✓ | ✓ | | | |
| 40 Gy at 8 Gy per fraction | ✓ | ✓ | ✓ | | | |
| 38.25 Gy at 7.25 Gy per fraction | ✓ | ✓ | ✓ | | | |
| Brachytherapy Monotherapy | | | | | | |
| Iodine 125 implant at 145 Gy | ✓ | ✓ | ✓ | | | |
| Palladium 103 implant at 125 Gy | ✓ | ✓ | ✓ | | | |
| Cesium implant at 115 Gy | ✓ | ✓ | ✓ | | | |
| HDR 27 Gy at 13.5 Gy in 2 implants | ✓ | ✓ | ✓ | | | |
| HDR 38 Gy at 9.5 Gy BID in 2 implants | ✓ | ✓ | ✓ | | | |
| Combined EBRT and Brachytherapy (EBRT 45–50.4 Gy at 1.8–2.0 Gy/fx, unless otherwise noted) | | | | | | |
| Iodine 125 implant at 110–115 Gy | | | | ✓ ± 4 mo ADT | ✓ with 1-3 y ADT | ✓ with 1-3 y ADT |
| Palladium 103 implant at 90–100 Gy | | | | ✓ ± 4 mo ADT | ✓ with 1-3 y ADT | ✓ with 1-3 y ADT |
| Cesium implant at 85 Gy | | | | ✓ ± 4 mo ADT | ✓ with 1-3 y ADT | ✓ with 1-3 y ADT |
| HDR 21.5 Gy at 10.75 Gy x 2 | | | | ✓ ± 4 mo ADT | ✓ with 1-3 y ADT | ✓ with 1-3 y ADT |
| EBRT 37.5 Gy at 2.5 Gy + 12–15 Gy single HDR | | | | ✓ ± 4 mo ADT | ✓ with 1-3 y ADT | ✓ with 1-3 y ADT |

¹Active surveillance should be strongly considered

²“Good” or “Poor” prognostic is not strictly defined. Predictive nomograms and/or molecular testing can be used to prognosticate PSA persistence/recurrence, prostate cancer specific mortality and metastasis free survival after definitive external beam radiation therapy. Although the prognostic value has been established, the predictive value of these tests remains unknown.

³Prophylactic nodal radiation may be considered if estimate of nodal metastasis is high.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

[Continued](#)

High-Risk Prostate Cancer: Role of Radical Prostatectomy and Radiation Therapy

Robert Qi Judd Moul

Division of Urology, Department of Surgery and Duke Cancer Institute, Duke University Medical Center, Durham, NC, USA

Table 2. Selected studies comparing prostate-specific mortality (PCSM) of combined radiation therapy (RT) and androgen deprivation therapy (ADT) with that of RT only

| Study (year, type) [ref.] | High-risk definition | High-risk patients, total, n | High-risk patients per treatment, n | Length of ADT, months | Median follow-up, years | PCSM, % | Significance |
|----------------------------------|-----------------------------------------------------------------|------------------------------|---------------------------------------------------------------|-------------------------|----------------------------------|--------------------------------------|-------------------------------------------------|
| Bolla et al. (2002, RCT) [45] | cT3/T4 N0/N1 M0 cT1/T2 and World Health Organization grade 3 | 415 | RT + ADT = 207 RT = 208 | 36 | 5.5 | RT + ADT = 6 RT = 21 | p = 0.0001 |
| Pilepich et al. (2005, RCT) [46] | cT3 positive regional lymph node | 977 | RT + ADT = 488 RT = 489 | indefinite ^a | 7.6 (all) 11 (survivors) | RT + ADT = 16 RT = 22 | p = 0.0052 |
| Granfors et al. (2006, RCT) [47] | locally advanced disease stratification for T and N stages | 91 | RT + ADT = 45 RT = 46 | indefinite ^b | 9.7 (all) 16.5 (survivors) | RT + ADT = 36 RT = 57 | p = 0.03 (overall) p = 0.005 (N1 only) |
| Horwitz et al. (2008, RCT) [41] | cT2c-T4, N0, with PSA < 150 ng/ml | 1,554 | RT + short-term ADT (sADT) RT + long-term ADT (lADT) | 4 28 | 11.31 11.27 | RT + sADT = 16.1 RT + lADT = 11.3 | p = 0.0042 |

^aContinuous drug application.

^bOrchiectomy.

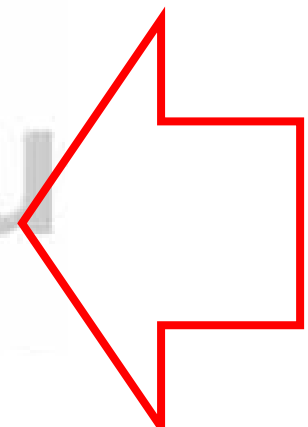
RCT = Randomized controlled trial; PSA = prostate-specific antigen.

High Risk

Men with prostate cancer that is clinical stage T3a, Gleason score 8 to 10/Gleason grade group 4-5, or PSA level greater than 20 ng/mL are categorized by the panel as high risk. Patients with multiple adverse factors may be shifted to the very high-risk category. The preferred treatment is EBRT in conjunction with 2 to 3 years of neoadjuvant/concurrent/adjvant ADT (category 1); ADT alone is insufficient. In particular, patients with low-volume, high-grade tumor warrant aggressive local radiation combined with typically 2 or 3 years of neoadjuvant/concurrent/adjvant ADT. Fit men in the high-risk group can consider 6 cycles of docetaxel without prednisone after EBRT is completed and while continuing ADT. The combination of EBRT and brachytherapy, with or without neoadjuvant/concurrent/adjvant ADT, is another primary treatment option. However, the optimal duration of ADT in this setting remains unclear.

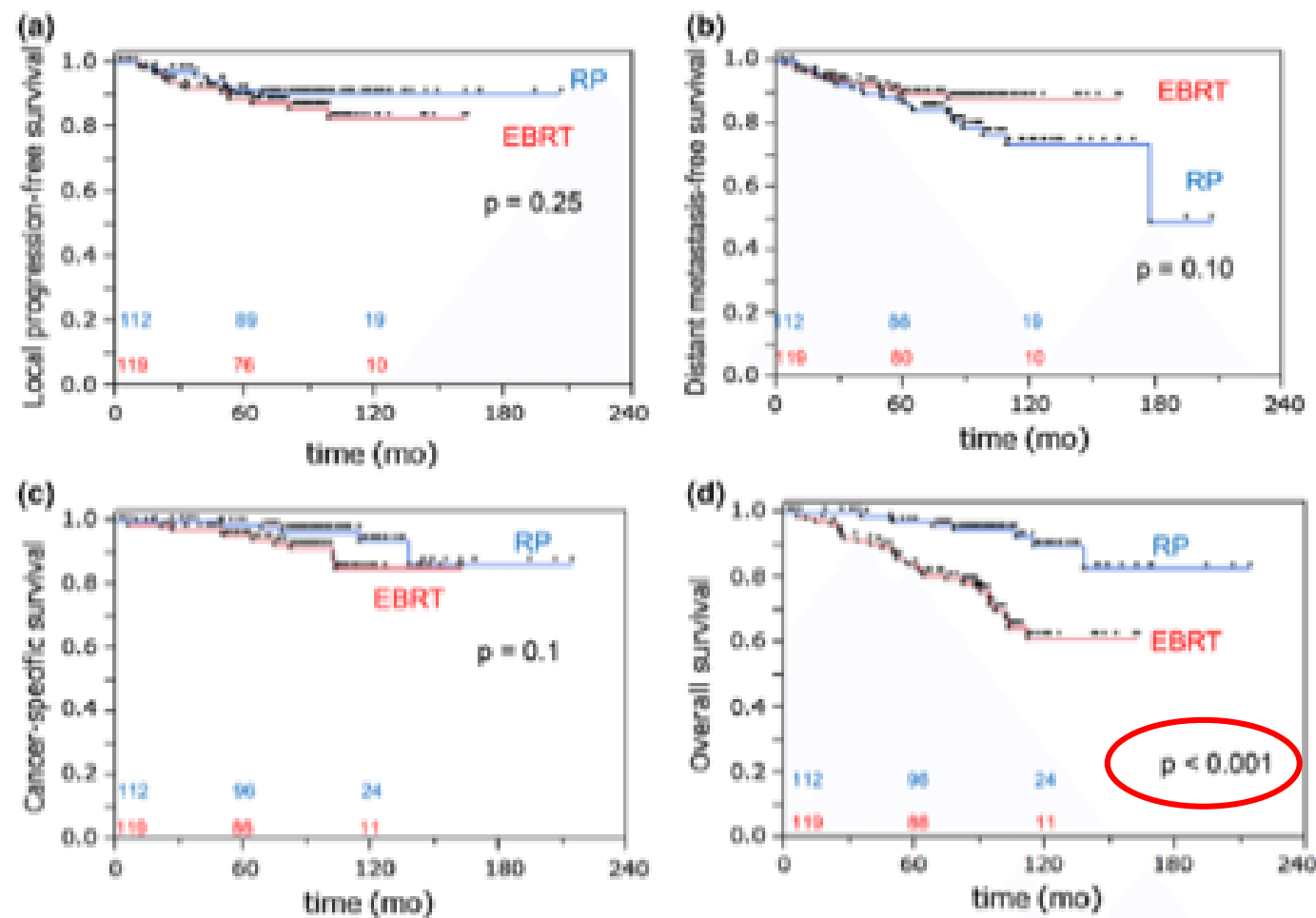
Radical prostatectomy with PLND remains an option because a subset of younger and healthier men in the high-risk group may benefit from operation.

Discu



Retrospective Comparison of External Beam Radiotherapy and Radical Prostatectomy in High-Risk, Clinically Localized Prostate

Arcangeli G, Strigari L, Arcangeli S, et al: Cancer. Int J Radiat Oncol 2009 Nov; 75(4): 975-982.



Kaplan-Meier local progression-free (a), distant metastasis free (b), cancer-specific (c) and overall (d) survival curves of patients with clinical T3 prostate cancer treated by radical prostatectomy (RP)

Comparison on efficacy of radical prostatectomy versus external beam radiotherapy for the treatment of localized prostate cancer

Linyan Chen^{1,*}, Qingfang Li¹, Yexiao Wang¹, Yiwen Zhang^{1,*} and Xuele Ma¹

¹State Key Laboratory of Biotherapy and Cancer Center, West China Hospital, Sichuan University and Collaborative Innovation Center, Chengdu, PR, China

Table 1: The main characteristics of included studies

| Author & Publication Year | Country (study interval) | Radiation Modality | Radiation dose (Gy) | Study Size (RP VS EBRT) | Age (RP VS EBRT) | Adjuvant Therapies (RP VS EBRT) | Salvage Therapies (RP VS EBRT) | Follow-up (RP VS EBRT) | Outcome |
|---------------------------|--------------------------|------------------------------|----------------------|-------------------------|------------------|---------------------------------|-------------------------------------------------|------------------------|---------------|
| Aizer 2009 | USA (1997-2005) | 3DCRT+IMRT (32%), IMRT (68%) | 75.6 | 204 VS 352 | 57.4 VS 68.4 | ADT: 3% VS 80% | - | 46 mo VS 60 mo | BDFS |
| Hamdy 2016 | UK (1999-2009) | 3DCRT | 74 | 553 VS 545 | 62 | - | RP: 0% VS 0.5% RT: 3% VS 0% ADT: 1% VS 3% | 10 yr | OS, CSS |
| Kibel 2012 | USA (1995-2005) | 3DCRT, IMRT | 74 | 6485 VS 2264 | 61 VS 70 | ADT: NA VS 34% | - | 67 mo | OS, CSS |
| Kim 2014 | Korea (2001-2011) | 3DCRT (79%), IMRT (21%) | 76 | 549 VS 189 | 66 VS 71 | ADT: 27% VS 69% | - | 48.8 mo VS 48.7 mo | OS, CSS, BDFS |
| Merino 2013 | Chile (1999-2010) | IMRT | 76 | 993 VS 207 | 63 VS 70 | ADT: 0% VS 42% | RT: 5% VS NA | 91.7 mo VS 76 mo | OS, CSS, BDFS |
| Nguyen 2008 | USA (1965-2002) | 3DCRT | 70.2 | 659 VS 288 | NA | ADT: 0% VS 0% | - | 5.6 yr | CSS |
| Shinozaki 2013 | Japan (2003-2006) | IMRT | 75 (65%), 70 (35%) | 48 VS 23 | 67 VS 69 | ADT: 0% VS 0% | - | 73 mo VS 65 mo | BDFS |
| Taguchi 2015 | Japan (2005-2012) | 3DCRT (6%), IMRT (94%) | 76 | 569 VS 322 | 66 VS 70 | ADT: 24% VS 69.3% | RP: 0% VS 0% RT: 5% VS 0% ADT: 12% VS 7% | 53 mo VS 45 mo | OS, CSS, BDFS |
| Takizawa 2009 | Japan (1998-2004) | 3DCRT | 70-71 | 86 VS 76 | 64.9 VS 71.1 | ADT: 83% VS 92% | - | 5 yr | BDFS |
| Yamamoto 2013 | Japan (1994-2005) | 3DCRT | 70 | 112 VS 119 | 67 VS 72 | ADT: 2% VS 21% | RP: 0% VS 0% RT: 5% VS 0% ADT: 31% VS 27% | 93 mo VS 85 mo | OS, CSS |
| Yamamoto 2016 | Japan (2007-2013) | 3DCRT (35%), IMRT (64%) | 70-78 | 71 VS 43 | 70 VS 73 | ADT: 0% VS 100% | - | 59.1 mo VS 54.5 mo | BDFS |
| Zelefsky 2010 | USA (1993-2002) | IMRT | 81 (79%), 86.4 (21%) | 1318 VS 1062 | 60 VS 69 | ADT: 1% VS 56% | RP: 0% VS 0.3% RT: 4% VS 0% ADT: 4% VS 8% | 5.1 yr VS 5.0 yr | CSS |

Abbreviations: RP: radical prostatectomy; EBRT: external beam radiotherapy; 3DCRT: three-dimensional conformal radiotherapy; IMRT: intensity-modulated radiation therapy; ADT: androgen deprivation therapy; OS: overall survival; CSS: cancer-specific survival; BDFS: biochemical disease-free survival; NA: not available.

Comparison on efficacy of radical prostatectomy versus external beam radiotherapy for the treatment of localized prostate cancer

Linyan Chen^{1,*}, Qingfang Li¹, Yexiao Wang¹, Yiwen Zhang^{1,*} and Xuelei Ma¹

¹State Key Laboratory of Biotherapy and Cancer Center, West China Hospital, Sichuan University and Collaborative Innovation Center, Chengdu, PR. China

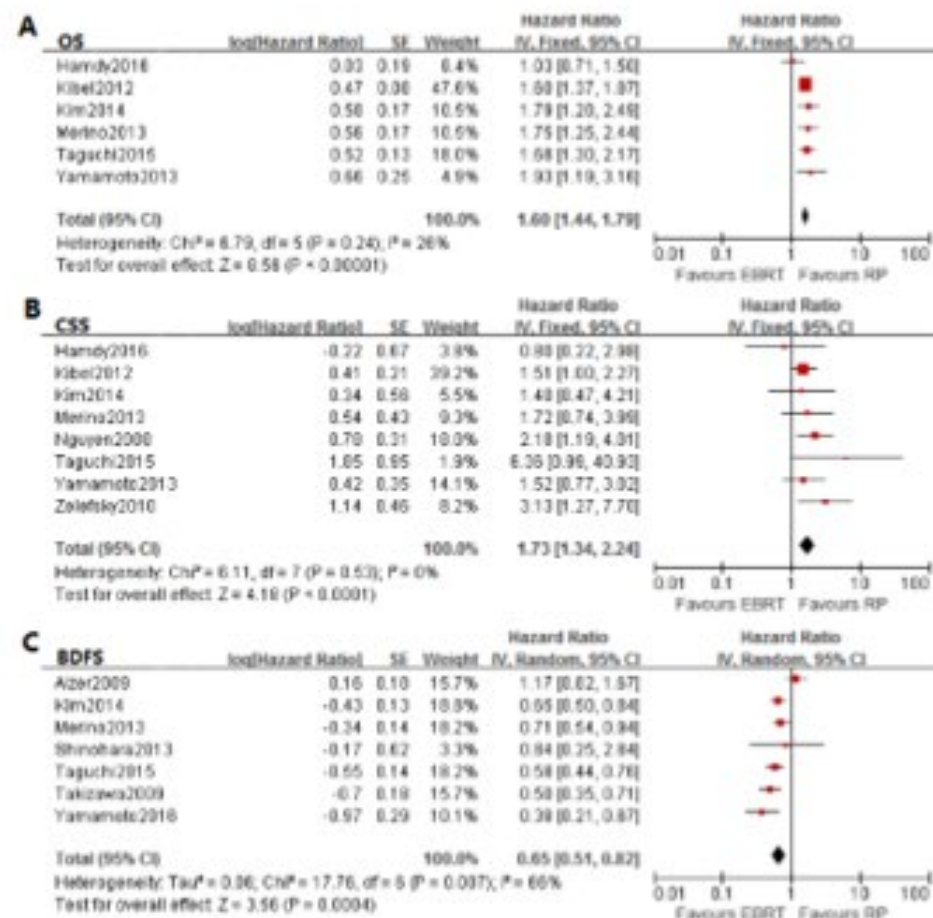


Figure 2: Forest plots of hazard ratio (HR) for overall survival (OS) (A), cancer-specific survival (CSS) (B), and biochemical disease-free survival (BDFS) (C).

Comparison on efficacy of radical prostatectomy versus external beam radiotherapy for the treatment of localized prostate cancer

Linyan Chen^{1,*}, Qingfang Li¹, Yexiao Wang¹, Yiwen Zhang^{1,*} and Xuele Ma¹

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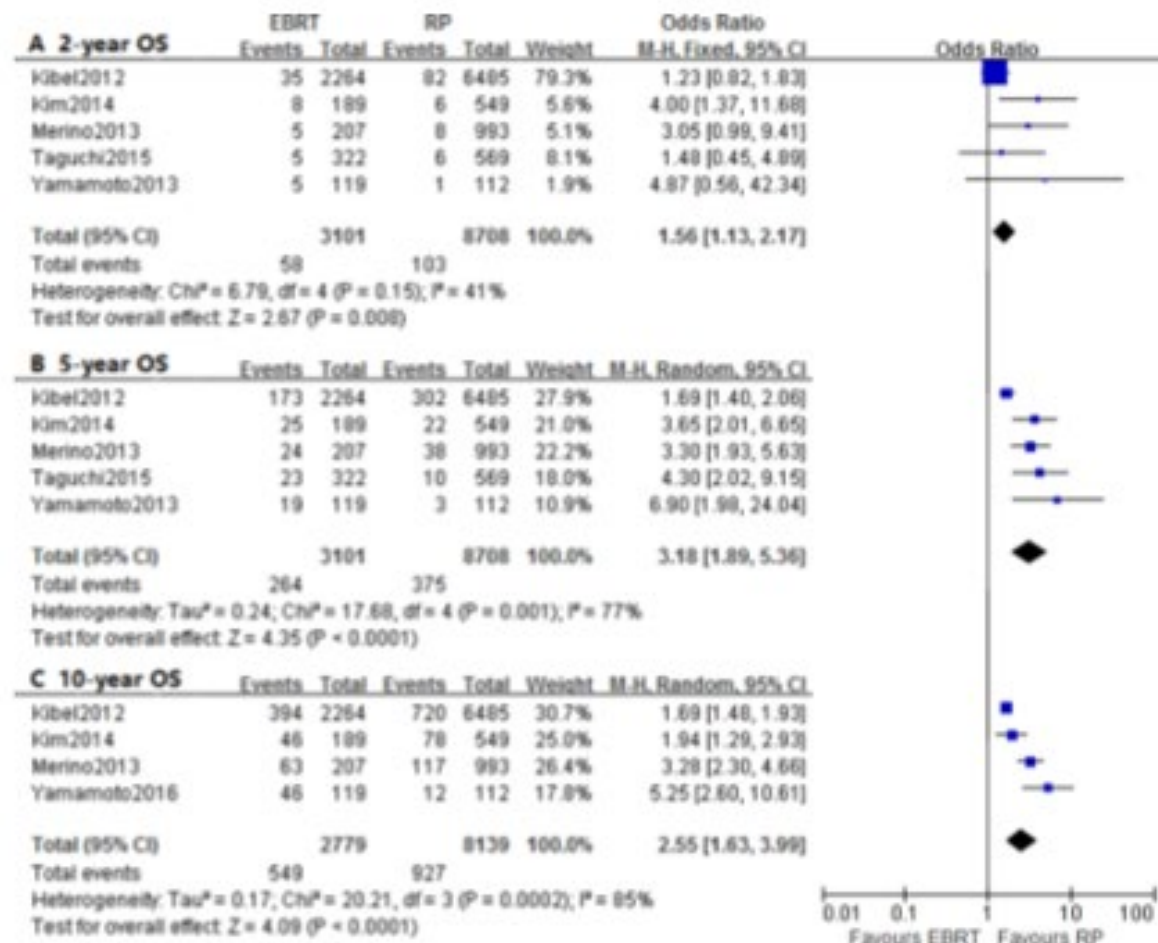
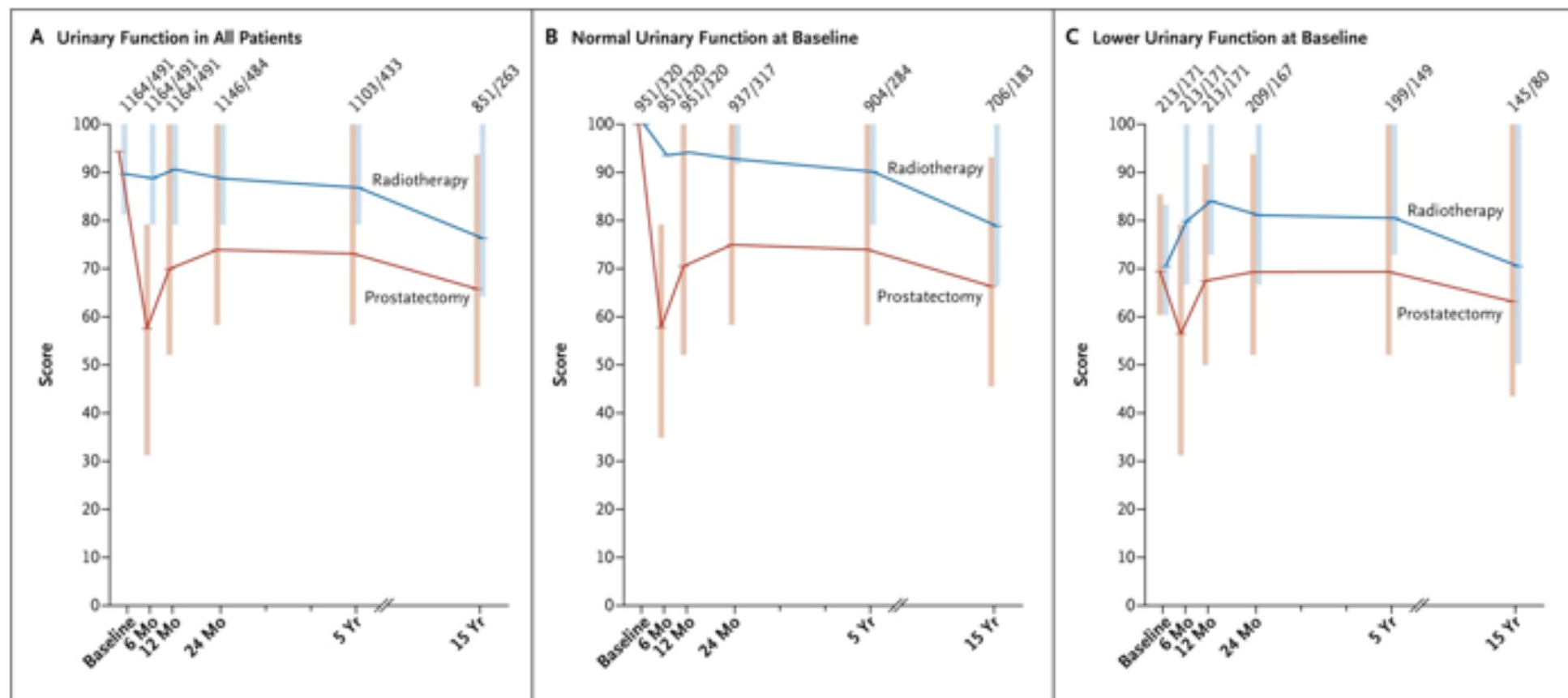


Figure 3: Forest plots of odd ratio (OR) for 2-year (A), 5-year (B) and 10-year (C) overall survival (OS).

[N Engl J Med](#). 2013 Jan 31;368(5):436-45. doi: 10.1056/NEJMoa1209978.

Long-term functional outcomes after treatment for localized prostate cancer.

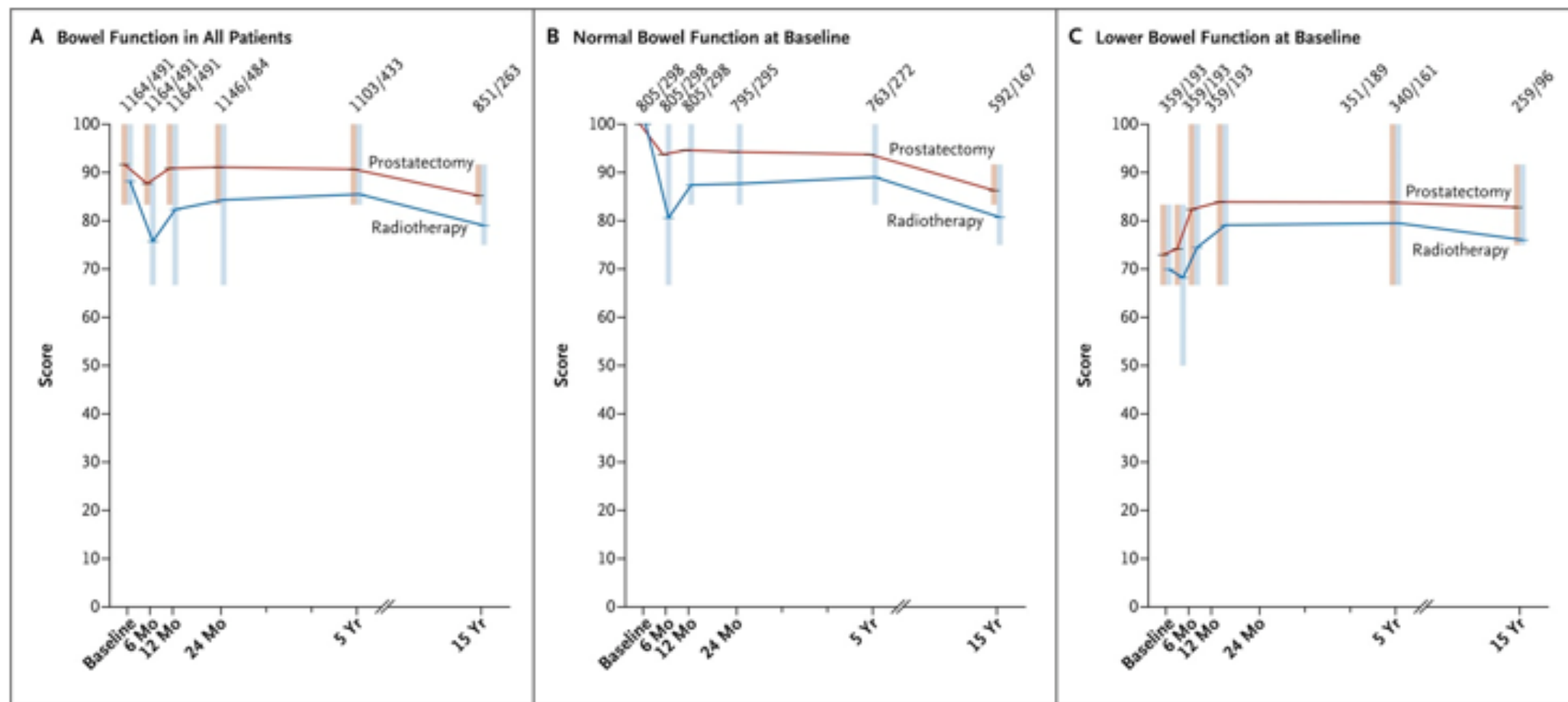
[Resnick MJ](#)¹, [Koyama T](#), [Fan KH](#), [Albertsen PC](#), [Goodman M](#), [Hamilton AS](#), [Hoffman RM](#), [Potosky AL](#), [Stanford JL](#), [Stroup AM](#), [Van Horn RL](#), [Penson DF](#).



scores for urinary function in the overall cohort (Panel A), in a subgroup of men with normal urinary function at baseline (summary score, 100) (Panel B), and in a subgroup of men with lower urinary function at baseline (summary score, <100) (Panel C)

Long-term functional outcomes after treatment for localized prostate cancer.

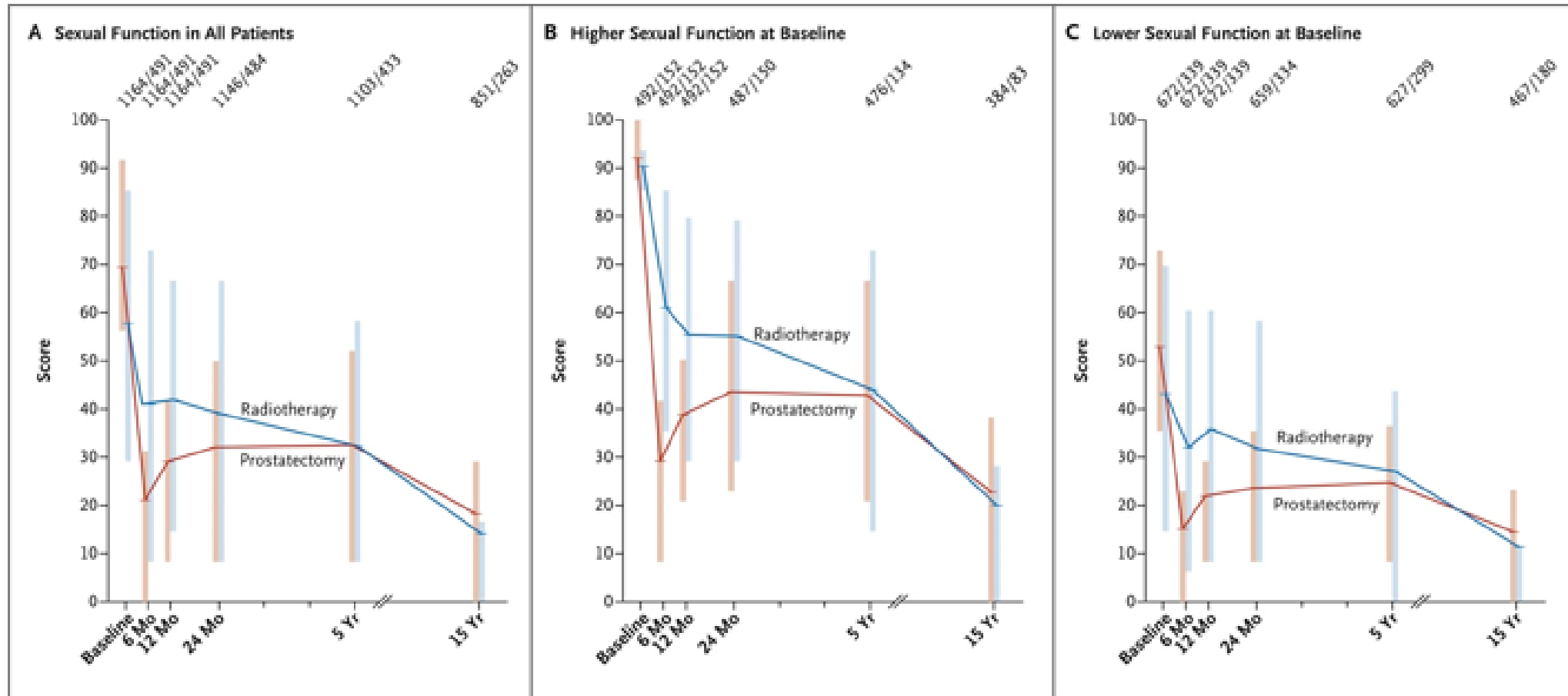
[Resnick MJ](#)¹, [Koyama T](#), [Fan KH](#), [Albertsen PC](#), [Goodman M](#), [Hamilton AS](#), [Hoffman RM](#), [Potosky AL](#), [Stanford JL](#), [Stroup AM](#), [Van Horn RL](#), [Penson DF](#).



bowel function in the overall cohort (Panel A), in a subgroup of men with normal bowel function at baseline (summary score, 100) (Panel B), and in a subgroup of men with lower bowel function at baseline (summary score, <100) (Panel C).

Long-term functional outcomes after treatment for localized prostate cancer.

[Resnick MJ](#)¹, [Koyama T](#), [Fan KH](#), [Albertsen PC](#), [Goodman M](#), [Hamilton AS](#), [Hoffman RM](#), [Potosky AL](#), [Stanford JL](#), [Stroup AM](#), [Van Horn RL](#), [Penson DF](#).



sexual function in the overall cohort (Panel A), in a subgroup of men with higher sexual function at baseline (summary score, greater than or equal to 80) (Panel B), and in a subgroup of men with lower sexual function at baseline (summary score, <80) (Panel C).

Adjuvant radiotherapy (ART) is defined as the administration of RT to post-prostatectomy

patients at a higher risk of recurrence

because of adverse pathological features prior to evidence of disease recurrence (i.e., with an undetectable PSA). There is no evidence that addresses the timing of the first PSA test post-prostatectomy to determine a patient's disease status; in the Panel's clinical experience the first PSA generally should be obtained two to three months post-RP.

**ART is usually administered within four to six months following RP.
Generally, RT is initiated after the return of acceptable urinary control.**

As sexual function can require one to two years before a full return of function is observed, return of erections is not a requirement before initiation of adjuvant radiation.

Physicians should offer adjuvant radiotherapy to patients with adverse pathologic findings at prostatectomy including

seminal vesicle invasion,
positive surgical margins, or
extraprostatic extension

because of demonstrated reductions

in biochemical recurrence,
local recurrence and
clinical progression.

(Standard; Evidence Strength: Grade A)

development of a PSA recurrence after surgery is associated with a higher risk of development of

metastatic prostate cancer or death from the disease.

Congruent with this clinical principle, physicians should regularly monitor PSA after radical prostatectomy to enable

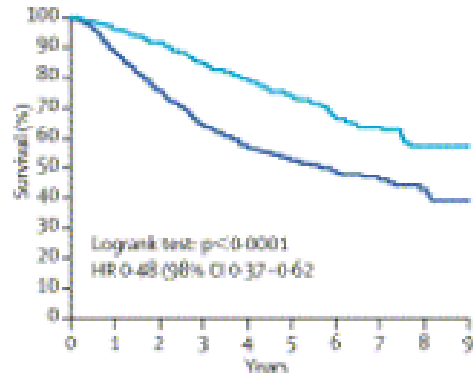
early administration of salvage therapies

if appropriate. (Clinical Principle)

effectiveness of radiotherapy for PSA recurrence is greatest when

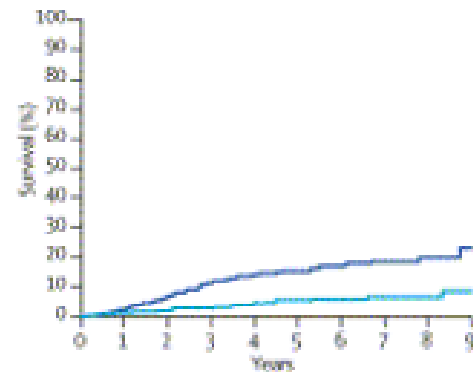
given at lower levels of PSA. (Clinical Principle)

Postoperative radiotherapy after radical prostatectomy: a randomised controlled trial (EORTC trial 22911) Prof Michel Bolla, MD



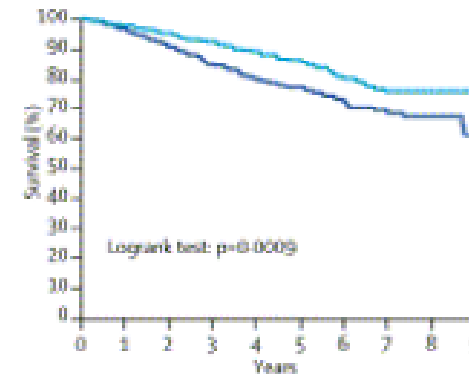
| Events | Patients | Number of patients at risk |
|--------|----------|----------------------------------|
| 220 | 503 | 425 337 243 182 126 84 52 27 10 |
| 134 | 503 | 456 407 330 262 193 125 85 41 11 |

biochemical progression-free survival was significantly improved in the irradiated group (74.0%, vs 52.8%, $p < 0.0001$).



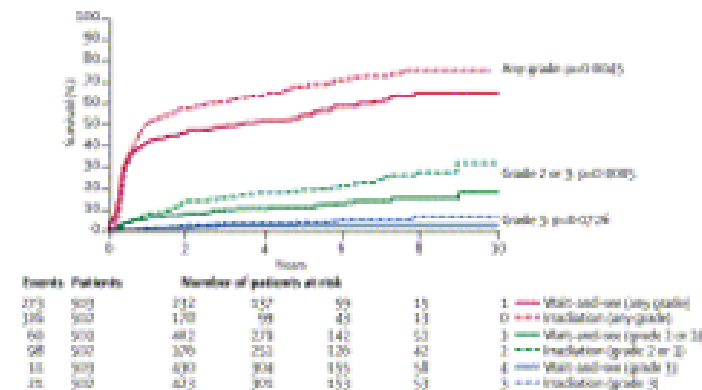
| Events | Patients | Number of patients at risk |
|--------|----------|-----------------------------------|
| 74 | 503 | 468 404 330 268 194 138 82 44 16 |
| 25 | 503 | 465 426 362 298 228 154 107 55 14 |

severe toxic toxicity (grade 3 or higher) were rare



| Events | Patients | Number of patients at risk |
|--------|----------|-----------------------------------|
| 113 | 503 | 467 401 324 259 188 124 79 42 16 |
| 75 | 503 | 464 424 357 291 221 150 101 53 14 |

locoregional failure was significantly lower in the irradiated group ($p < 0.0001$)



Adjuvant radiotherapy for pathologically advanced prostate cancer: a randomized clinical trial. Thompson IM, Tangen CM, Paradelo J, et al. JAMA 2006;296:2329-35.

data from the SWOG 8794/PR-2 trial indicated only short-term toxicity with early adjuvant radiotherapy, which was well tolerated.

Grade 1 or 2 gastrointestinal toxicity at 6 weeks occurred in **59%** of patients in the radiotherapy group versus **7%** in the observation group (**p < 0.001**), but at 5 years, there was no difference **11% v. 19%**, (p = 0.16).

Similarly, genitourinary toxicity occurring at 6 weeks was 37% versus 18% (**p = 0.004**) and at 5 years, there was no difference **23% v. 18%**, (p = 0.55).

ΣΥΜΠΛΗΡΩΜΑΤΙΚΗ ΑΚΤΙΝΟΘΕΡΑΠΕΙΑ ΜΕΤΑ ΑΠΌ ΠΡΟΣΤΑΤΕΚΤΟΜΗ

| | bRFS | LRR | HTFS | ClinR | MetR | OS |
|----------------------|----------------------|----------------|-----------------|--------------|-------------|-------------|
| SWOG 8794 | SS | 8-22 p<0,01 | 84-66 SS | P=0,054 | 71-61 SS | 74-66 SS |
| EORTC 22911 | SS | 8,4-17,3 SS | 21,8-47,5 SS | ? | NS | NS |
| ARO 96-02 | SS | | | | | |
| META ANALYSIS | HR:0,48 p<0,00001 | | | | | |

Salvage radiotherapy (SRT) is defined as the administration of RT to the prostatic bed and possibly to the surrounding tissues, including lymph nodes,

in the patient with a PSA recurrence

after surgery but no evidence of distant metastatic disease. Biochemical (PSA) recurrence after surgery is defined as a detectable PSA level ≥ 0.2 ng/mL with a second confirmatory level ≥ 0.2 ng/mL



Platinum Priority – Collaborative Review – Prostate Cancer
Editorial by Christopher C. Parker and Matthew R. Sydes on pp. 1044–1045 of this issue

Early Salvage Radiotherapy Following Radical Prostatectomy

David Pfister^{a,*}, Michel Bolla^b, Alberto Briganti^c, Peter Carroll^d, Cesare Cozzarini^e, Steven Joniau^f,
Hein van Poppel^g, Mack Roach^h, Andrew Stephenson^h, Thomas Wiegelⁱ, Michael J. Zelefsky^j

Early salvage RT after RP is an effective treatment, with favourable outcomes for patients with pre-RT PSA levels <0.5 ng/ml, but only retrospective data from heterogeneously designed studies are available to support our notion at this point.

Table 1 – Ongoing prospective trials on salvage radiation therapy (RT), early salvage RT, and adjuvant RT and hormone treatment

| Trial | Design | Arms | Pts | Intention | Dosage, Gy | Primary end points | Secondary end points |
|-------------------|-------------------------------------------------------------------|-----------------------------------------------------------------|------|------------------------------------------|-----------------------------------------------|-----------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| RADICALS RT | International, multicentre, open-labelled, randomised, controlled | Adjuvant vs Deferred RT (PSA failure) | 1150 | RT | 66 Gy in 33 fractions 52.5 in 20 fractions | Freedom from distant disease PCa mortality | PCa-specific survival Freedom from treatment failure Clinical PFS OS Nonprotocol hormone therapy Treatment toxicity Patient-reported outcomes |
| RADICALS HD | International, multicentre, open-labelled, randomised, controlled | No hormones, short-term ADT (6 mo) vs long-term ADT (24 mo) | 2000 | Hormones | 66 Gy in 33 fractions | PCa-specific survival | Freedom from distant metastases (any distant metastases or PCa-specific death) Freedom from treatment failure Clinical PFS OS Nonprotocol hormone therapy Treatment toxicity Patient-reported outcomes |
| GETUG-17 | Multicentre, open-labelled, randomised, controlled | Adjuvant RT vs early salvage RT (PSA >0.2 ng/ml) | 718 | RT and hormones (6 mo) | 66 Gy in 33 fractions | PFS (clinical or biochemical) | OS Metastasis-free survival Toxicity QoL Functional results in patients >75 yr of age |
| RAVES | Multicentre, open-labelled, randomised, controlled | Adjuvant RT vs early salvage RT (PSA >0.2 ng/ml) | 470 | RT Noninferiority of early salvage RT | 64 Gy in 32 fractions | PFS QoL | Toxicity OS PCa-specific survival Time to local failure Time to distant failure Time to ADT |
| EORTC 22043-30041 | Multicentre, open-labelled, randomised, controlled | Adjuvant RT vs early salvage RT (0.1 < PSA <0.5 ng/ml) plus ADT | 600 | RT and hormones | 64–74 Gy | bRFS | Toxicity, early/late Clinical PFS OS Distant metastasis-free survival QoL |

RADICALS – Radiotherapy and Androgen Deprivation in Combination After Local Surgery; RT – radiation therapy; PSA – prostate-specific antigen; PCa – prostate cancer; PFS – progression-free survival; OS – overall survival; ADT – androgen-deprivation therapy; QoL – quality of life; RAVES – Radiotherapy Adjuvant vs Early Salvage; EORTC – European Organisation for Research and Treatment of Cancer; bRFS – biochemical recurrence-free survival.

Early Salvage Radiotherapy Following Radical Prostatectomy

June 2014 European Urology 65(6):1034–1043

[David Pfister](#), [Michel Bolla](#), [Alberto Briganti](#), [Michael J. Zelefsky](#)

Evidence synthesis Patients treated with

- **early salvage RT have a significantly improved biochemical recurrence-free survival (BRFS) rate**

compared with those receiving salvage RT initiated after PSA values are >0.5 ng/ml. Similarly, within the cohort of patients with pre-RT PSA values <0.5 ng/ml, improved BRFS rates were noted among those with

- **lower rather than higher pre-RT PSA levels.** It is possible that
- **higher RT dose levels and the use of adjunctive androgen-deprivation therapy improve biochemical control outcomes**

in the salvage setting. Conclusions Based on a literature review, improved 5-yr BRFS rates are observed for patients who receive early salvage RT compared with patients treated with salvage RT with a pre-RT PSA value >0.5 ng/ml. Whether the routine application of early salvage RT in patients with initially undetectable PSA levels will be associated with demonstrable clinical benefit awaits the results of ongoing prospective trials.

[Rev Urol](#). 2002 Spring; 4(2): 87–89.

PMCID: PMC1475975

PMID: [16985660](#)

Radiation Therapy After Radical Prostatectomy: Strike Early, Strike Hard! The Case for Adjuvant Radiation Therapy

[Dov Kadmon](#), MD

Main Points

- Over 90% of patients whose tumors are confined to the prostate have 5-year disease-free survival; patients with positive surgical margins have a 28%–49% incidence of biochemical failure within 5 years of surgery.
- **Most patients whose cancer recurs within 2 years of surgery and whose serum prostate-specific antigen (PSA) rises rapidly develop clinical metastases, with or without local recurrences.**
- **Patients whose serum PSA becomes detectable more than 2 years after surgery and who display a slow PSA rise present predominantly with local recurrences.**
- Radiotherapy given when patients develop palpable local recurrences is rarely, if ever, effective; when “salvage” radiotherapy is given because of a detectable serum PSA
the lower the serum PSA level before radiotherapy, the better the outcome.

A Phase III trial to investigate the timing of radiotherapy for prostate cancer with high-risk features: background and rationale of the Radiotherapy – Adjuvant Versus Early Salvage (RAVES) trial

[Maria Pearse](#), [Carol Fraser-Browne](#), [Ian D. Davis](#), [Gillian M. Duchesne](#), [Richard Fisher](#)

early salvage radiotherapy (SRT) is not inferior to 'standard' treatment with adjuvant RT (ART) with respect to biochemical failure in patients with pT3 disease and/or positive surgical margins (SMs) after radical prostatectomy (RP).

International collaborations have developed, including a planned meta-analysis to be undertaken with the UK Medical Research Council/National Cancer Institute of Canada Clinical Trials Group RADICALS (Radiotherapy and Androgen Deprivation In Combination with Local Surgery) trial and an innovative psycho-oncology sub-study to investigate a patient decision aid resource.

On the current evidence available, it

remains unclear if ART is equivalent or superior to observation with early SRT.

Predicting the outcome of salvage radiation therapy for recurrent prostate cancer after radical prostatectomy:

Stephenson AJ, Scardino PT, Kattan MW, Pisansky TM, Slawin KM, Klein EA, Anscher MS, Michalski JM, Sandler HM, Lin DW, Forman JD, Zelefsky MJ, Kestin LL, Roehrborn CG, Catton CN, DeWeese TL, Liauw SL, Valicenti RK, Kuban DA, Pollack A, *Glickman Urological Institute, Cleveland Clinic Foundation, Cleveland, OH*

The 6-year progression-free probability was 32% (95% CI, 28% to 35%) overall.

Significant variables in the model were:

PSA level before SRT ($P < .001$),
prostatectomy Gleason grade ($P < .001$),
PSA doubling time ($P < .001$),
[surgical margins](#) ($P < .001$),
[androgen-deprivation](#) therapy before or during SRT ($P < .001$),
[lymph node metastasis](#) ($P = .019$).

Conclusion

Nearly half of patients with recurrent prostate cancer after radical prostatectomy have a long-term **PSA response to SRT when treatment is administered at the earliest sign of recurrence.**

Αξιολόγηση κινδύνου

Genomic Classifier Identifies Men With Adverse Pathology After Radical Prostatectomy Who Benefit From Adjuvant Radiation Therapy

Robert B. Den, Kasra Yousefi, Edouard J. Trabulsi, Firas Abdollah, Voleak Choeurng, Felix Y. Feng, Adam P. Dicker, Costas D. Lallas, Leonard G. Gomella, Elai Davicioni, and R. Jeffrey Karnes

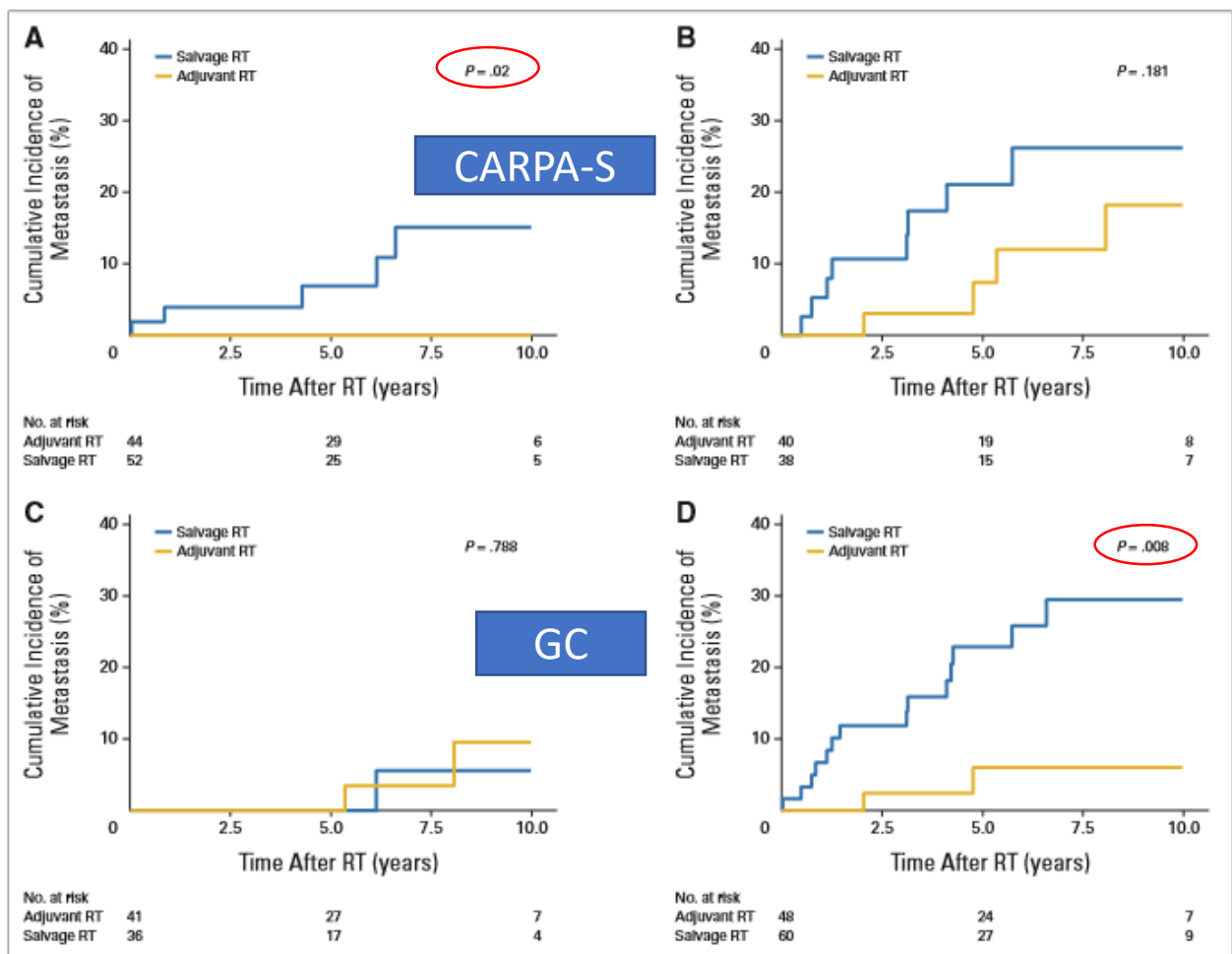


Fig 3. Cumulative incidence curves to evaluate benefit from adjuvant radiotherapy (RT) versus salvage RT stratified by (A and B) Cancer of the Prostate Risk Assessment Postsurgical (CAPRA-S) score and (C and D) genomic classifier (GC).

ΤΕΧΝΙΚΕΣ ΑΚΤΙΝΟΘΕΡΑΠΕΙΑΣ

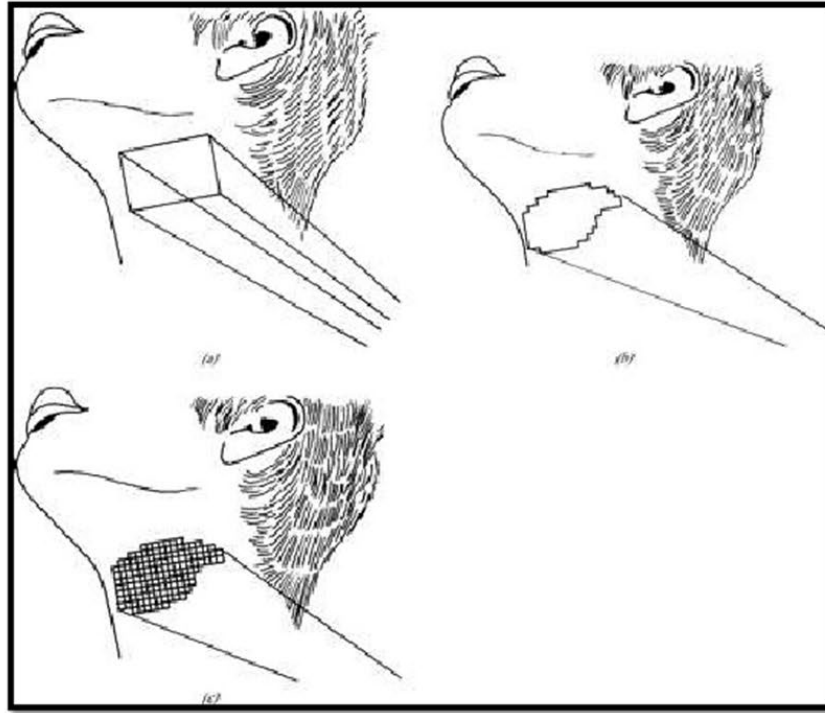
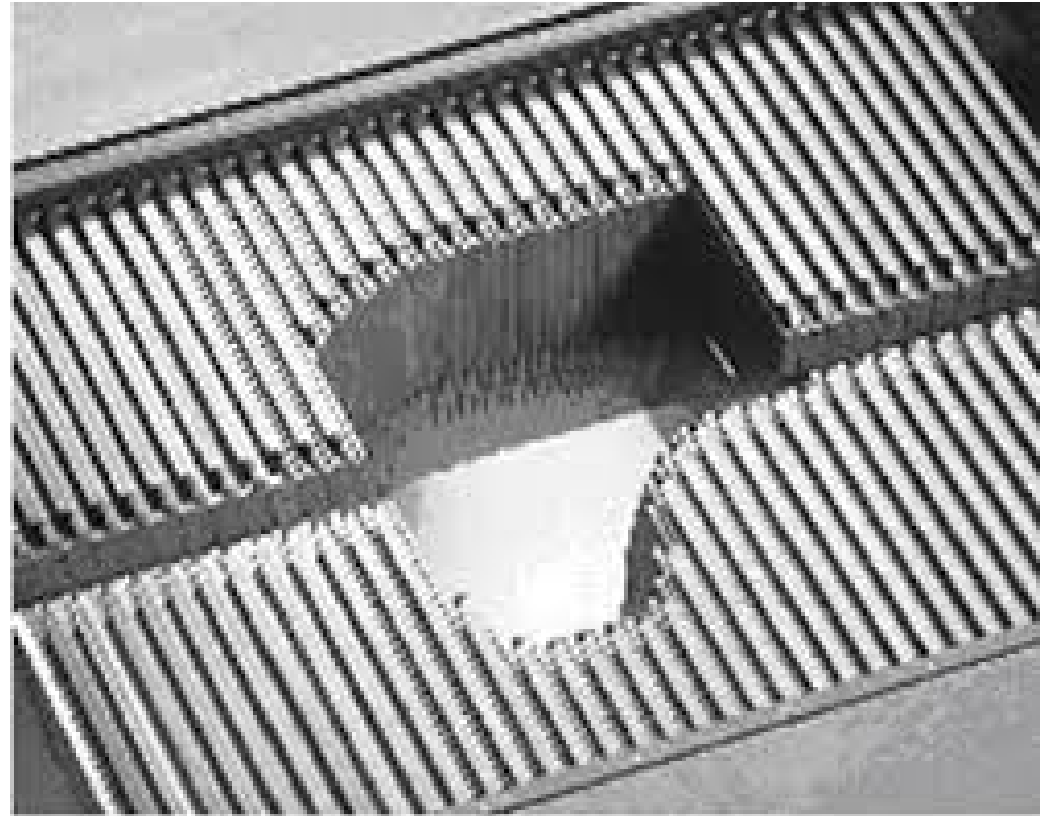
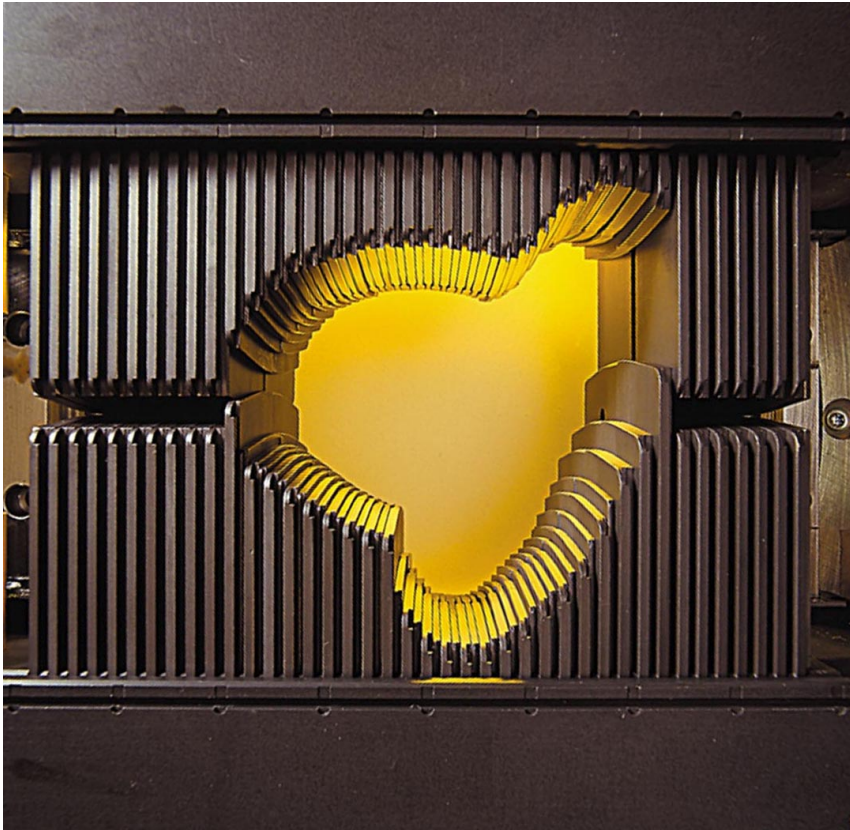


Figure: differences between
(a) conventional
radiotherapy,
(b) conformal radiotherapy
(CFRT) without intensity-
modulation and
(c) CFRT with intensity
modulation (IMRT).

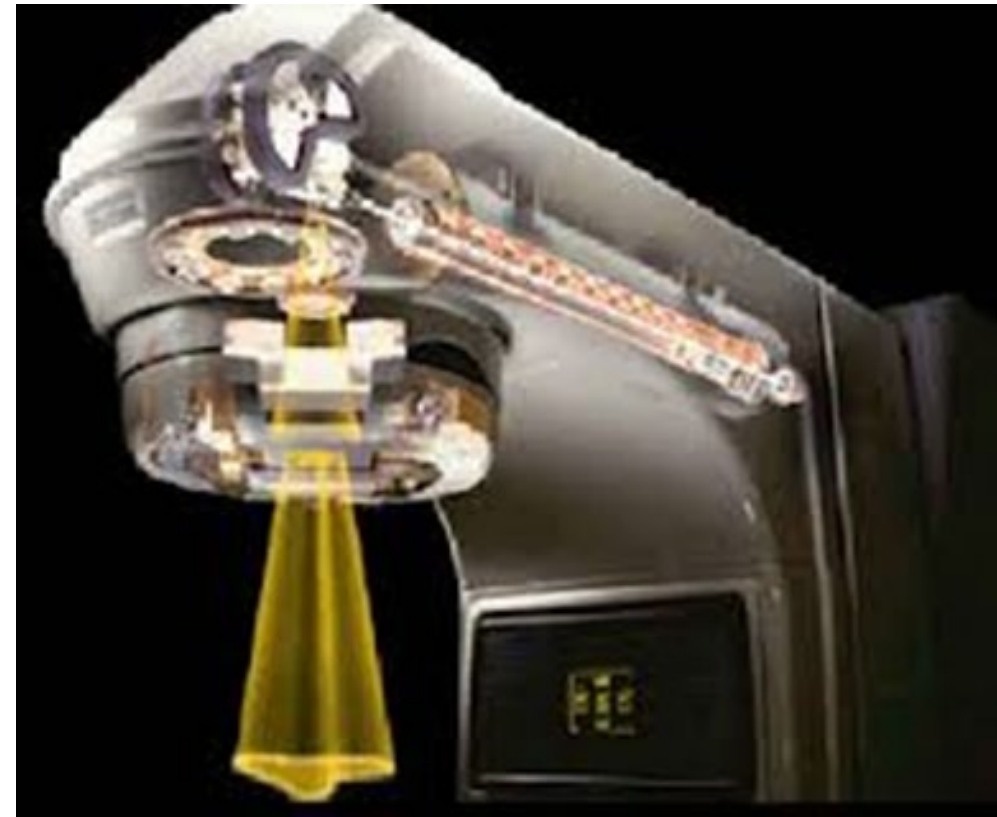
ΤΕΧΝΙΚΕΣ ΑΚΤΙΝΟΘΕΡΑΠΕΙΑΣ

- Ο κατευθυντήρας πολλαπλών φύλλων (mlc)



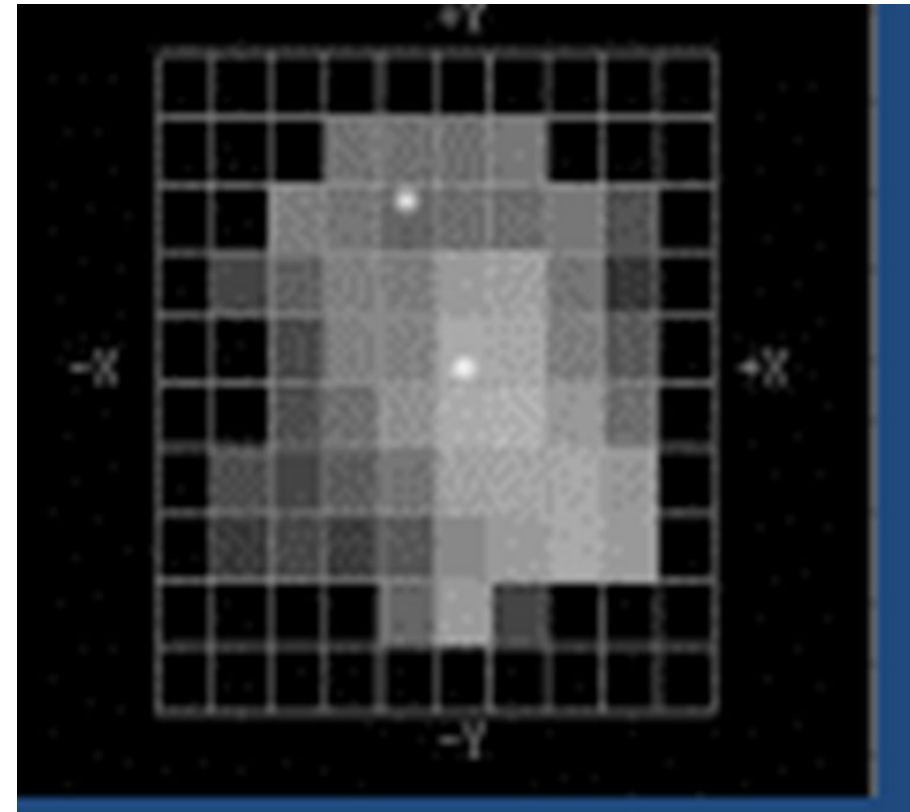
ΤΕΧΝΙΚΕΣ ΑΚΤΙΝΟΘΕΡΑΠΕΙΑΣ

- Η κεφαλή του Γραμμικού Επιταχυντή



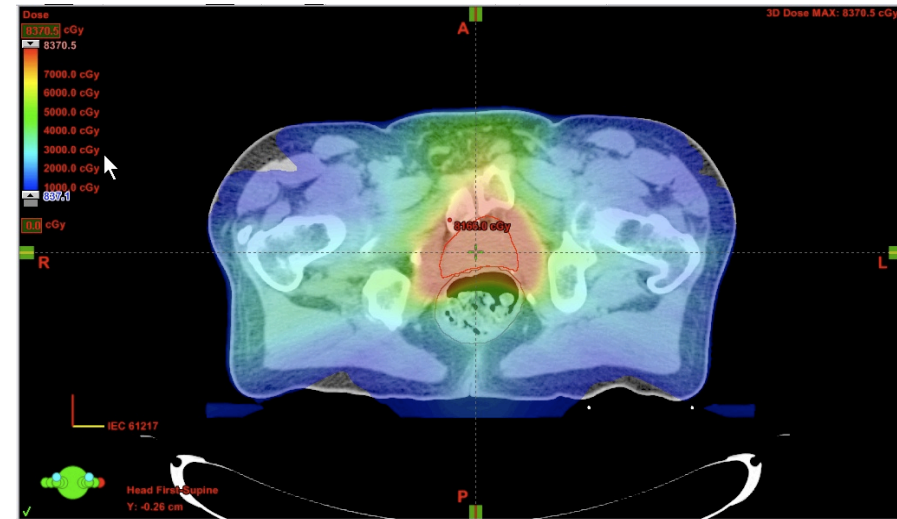
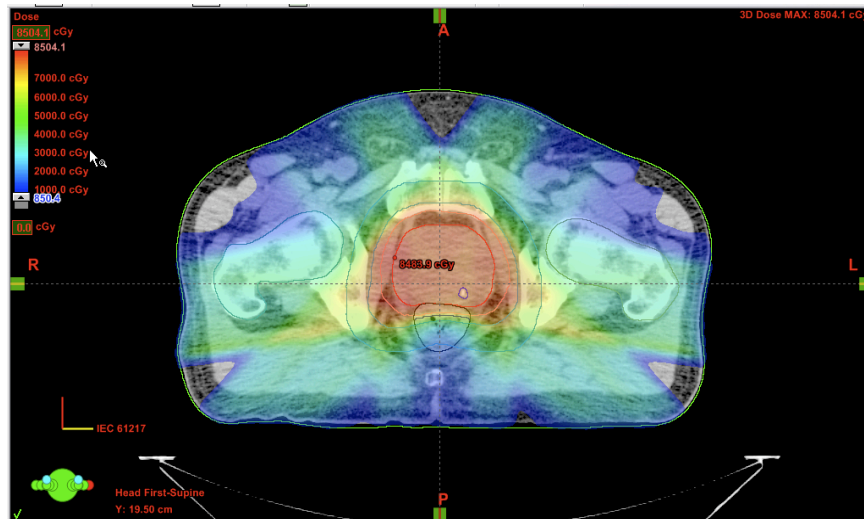
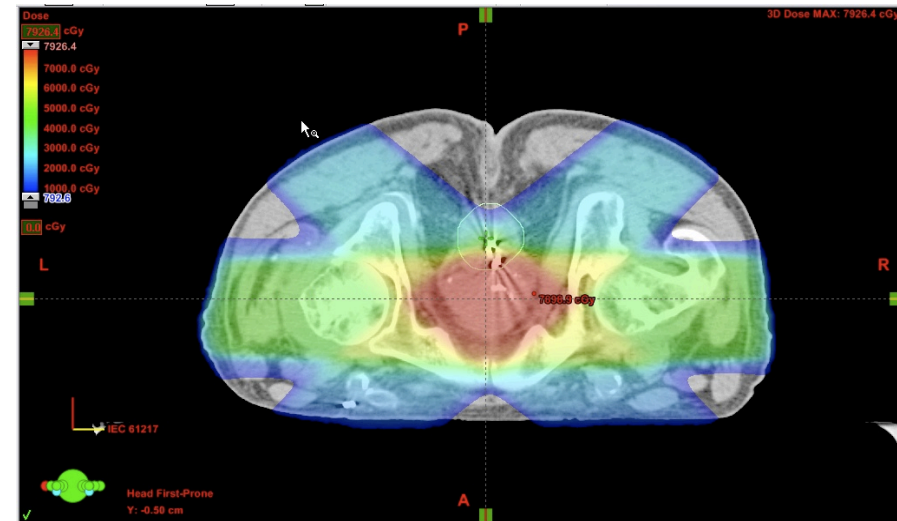
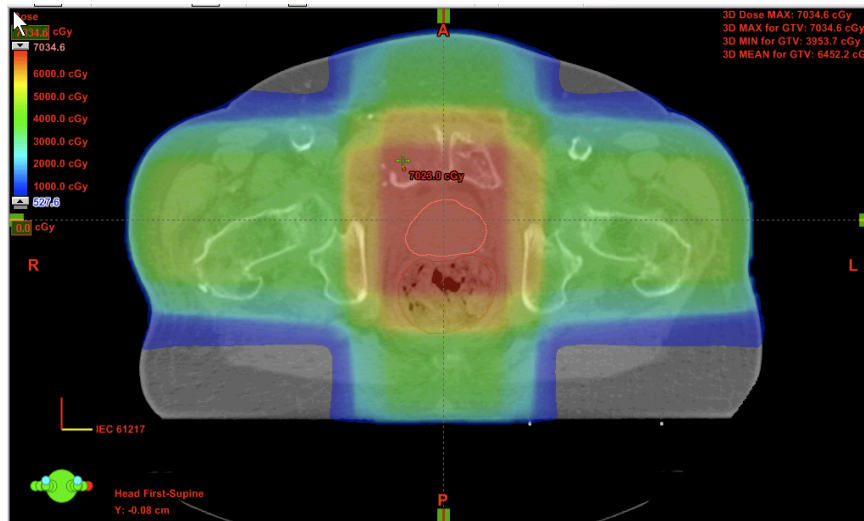
ΤΕΧΝΙΚΕΣ ΑΚΤΙΝΟΘΕΡΑΠΕΙΑΣ

- Το πεδίο χωρίζεται σε υποπεδία
- Κάθε υποπεδίο ακτινοβολείται διαφορετικό χρόνο
- Κάθε voxel στο χώρο θεραπείας δέχεται το άθροισμα της δόσης των υποπεδίων που το στοχεύουν.
- Το τελικό αποτέλεσμα είναι η «ιδανική» κατανομή δόσης

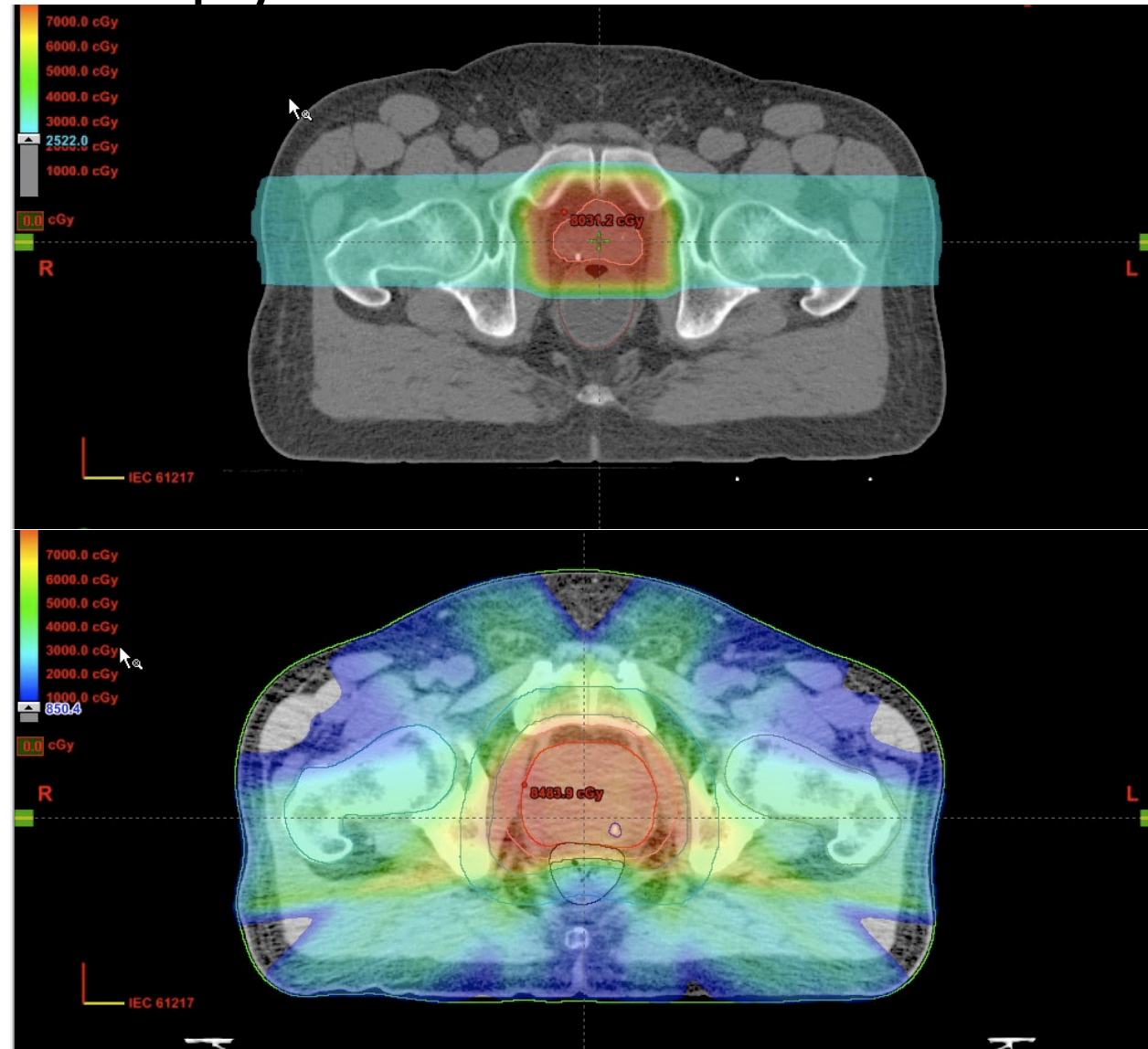


Κατανομή δόσης σε 2D-CRT(3D)-IMRT, IGRT

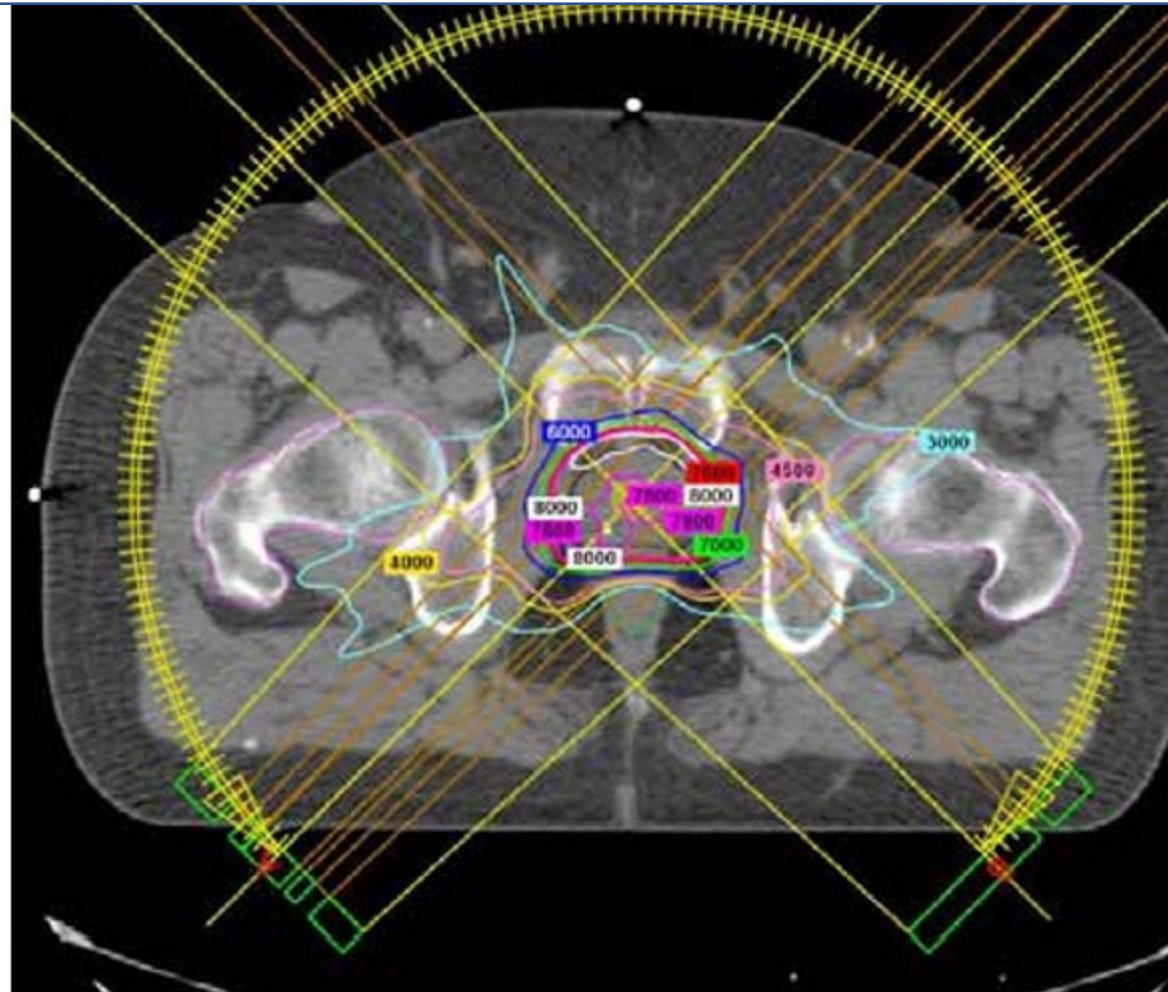
2D RT



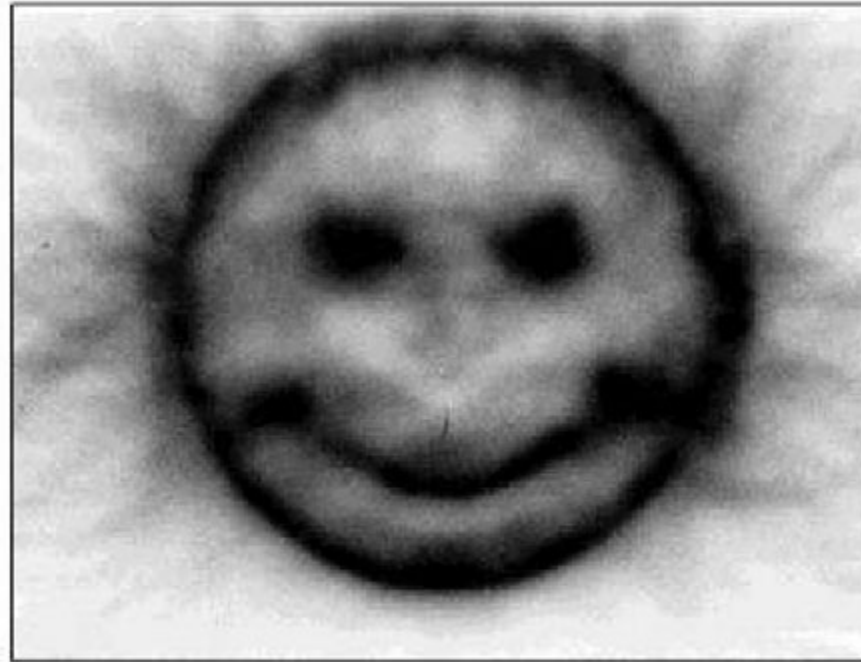
Proton Therapy vs. IMRT



ΤΕΧΝΙΚΕΣ ΑΚΤΙΝΟΘΕΡΑΠΕΙΑΣ

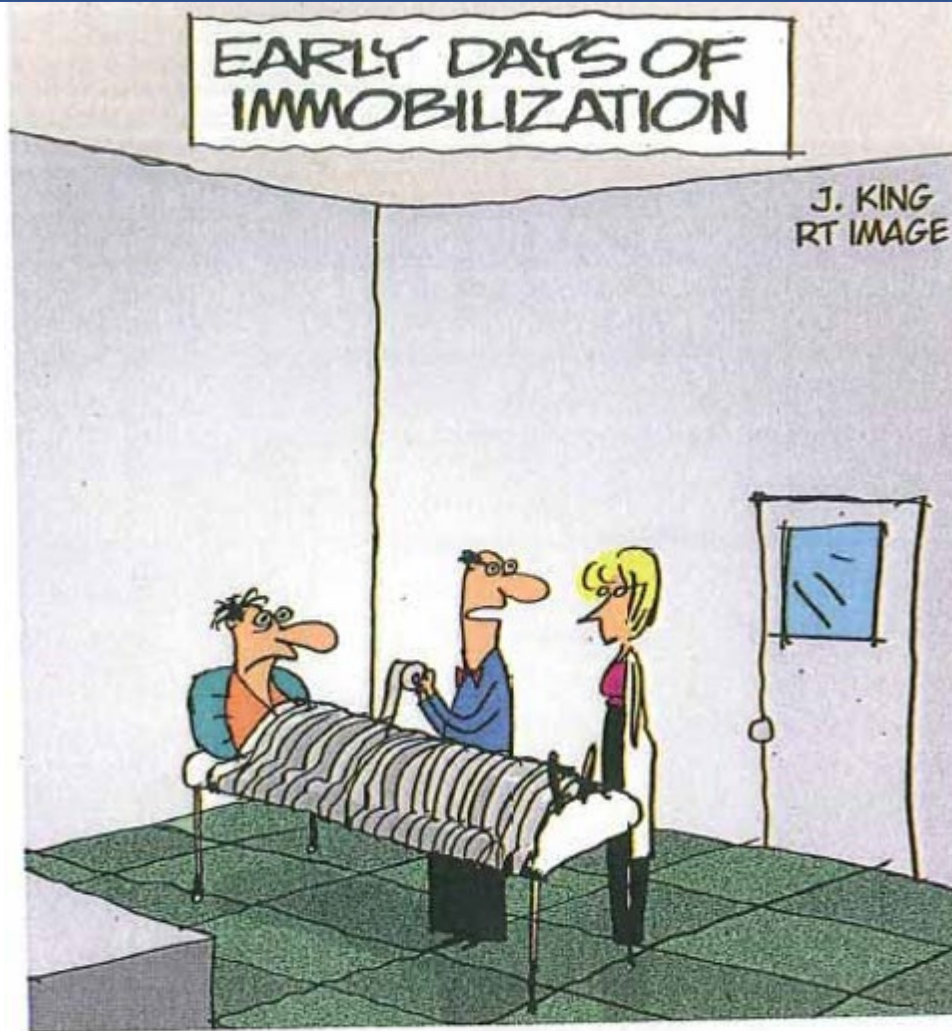


ΤΕΧΝΙΚΕΣ ΑΚΤΙΝΟΘΕΡΑΠΕΙΑΣ



*A smiling face demonstrating how radiation can be deposited
in almost any pattern.*

ΤΕΧΝΙΚΕΣ ΑΚΤΙΝΟΘΕΡΑΠΕΙΑΣ



"We're out of duct tape."

ΤΕΧΝΙΚΕΣ ΑΚΤΙΝΟΘΕΡΑΠΕΙΑΣ

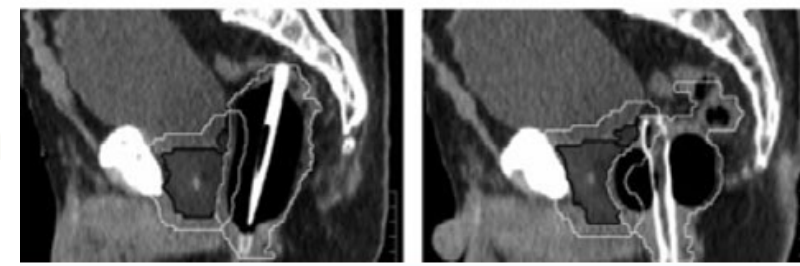
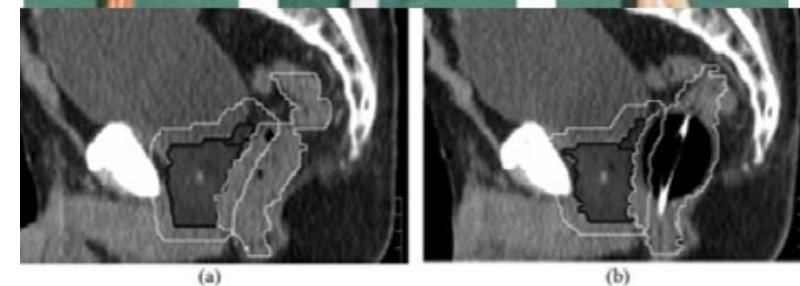
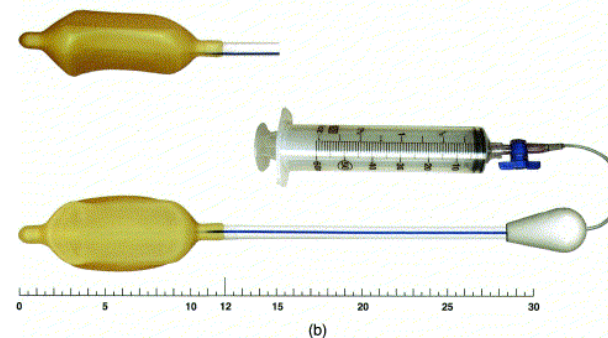
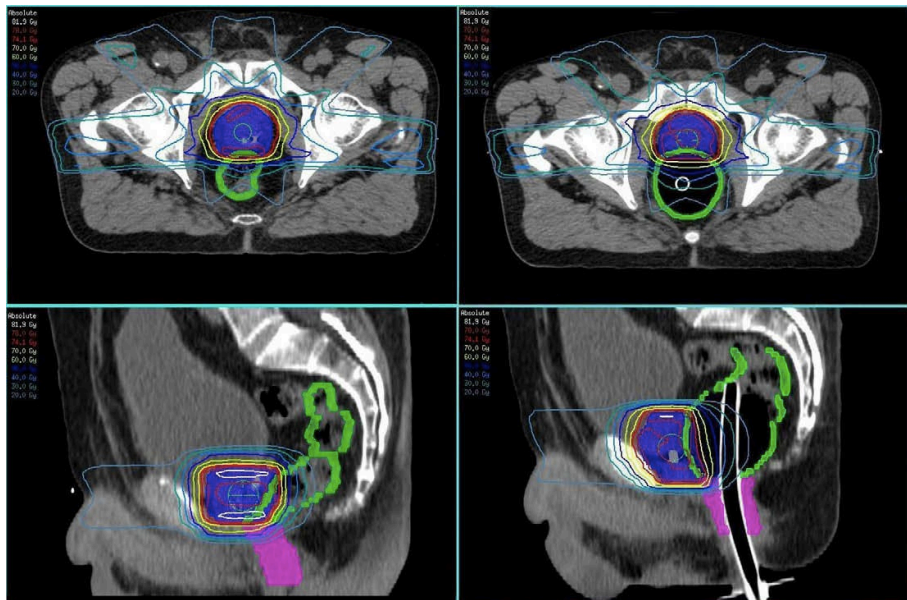
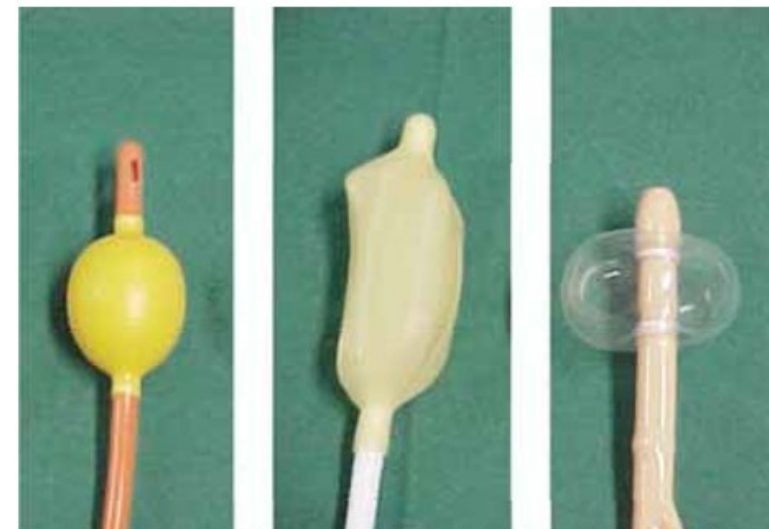
- Εξελιγμένα συστήματα σχεδιασμού της θεραπείας επιτυγχάνουν την «ιδανική» κατανομή, αλλά πως θα φτάσει στον στόχο;
- Οι μεγάλες δόσεις απαιτούν περιορισμένα πεδία για την άσκοπη έκθεση των γύρω φυσιολογικών ιστών
- Η εσωτερική κίνηση των οργάνων επιβάλλει την καθημερινή επιβεβαίωση του στόχου

ΤΕΧΝΙΚΕΣ ΑΚΤΙΝΟΘΕΡΑΠΕΙΑΣ

Ενδοορθικό μπαλόνι.

Τοποθετείται καθημερινά πριν από τη θεραπεία και διατείνεται με αέρα, ώστε να καθλώσει τον προστάτη πίσω από την ηβική σύμφυση

Teh, Red Journal 2001

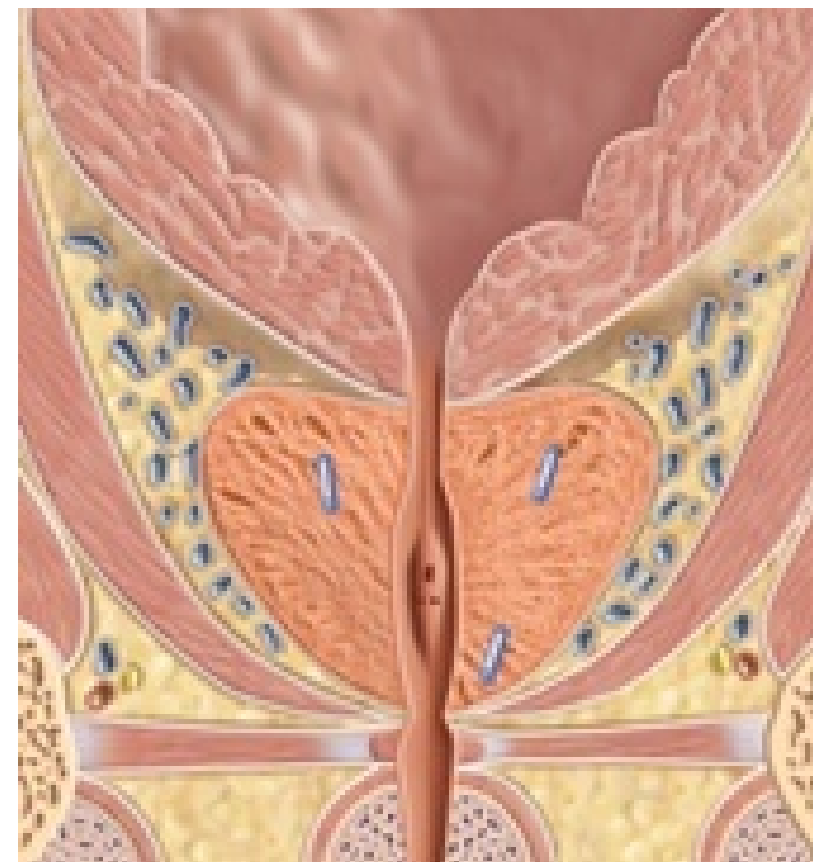
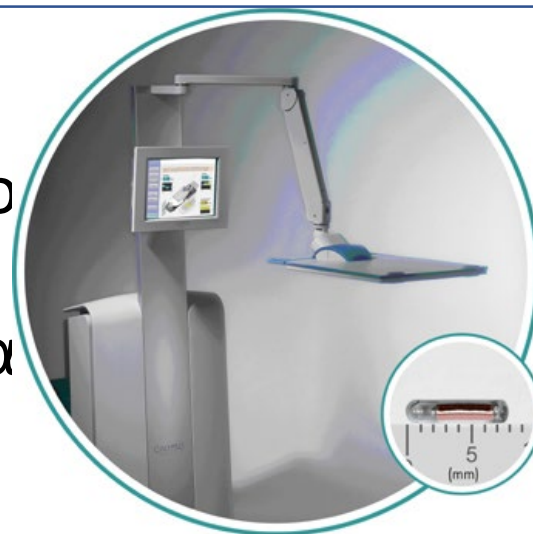


78 Gy πλάνο θεραπείας χωρίς ή με τοποθετημένο τον καθετήρα

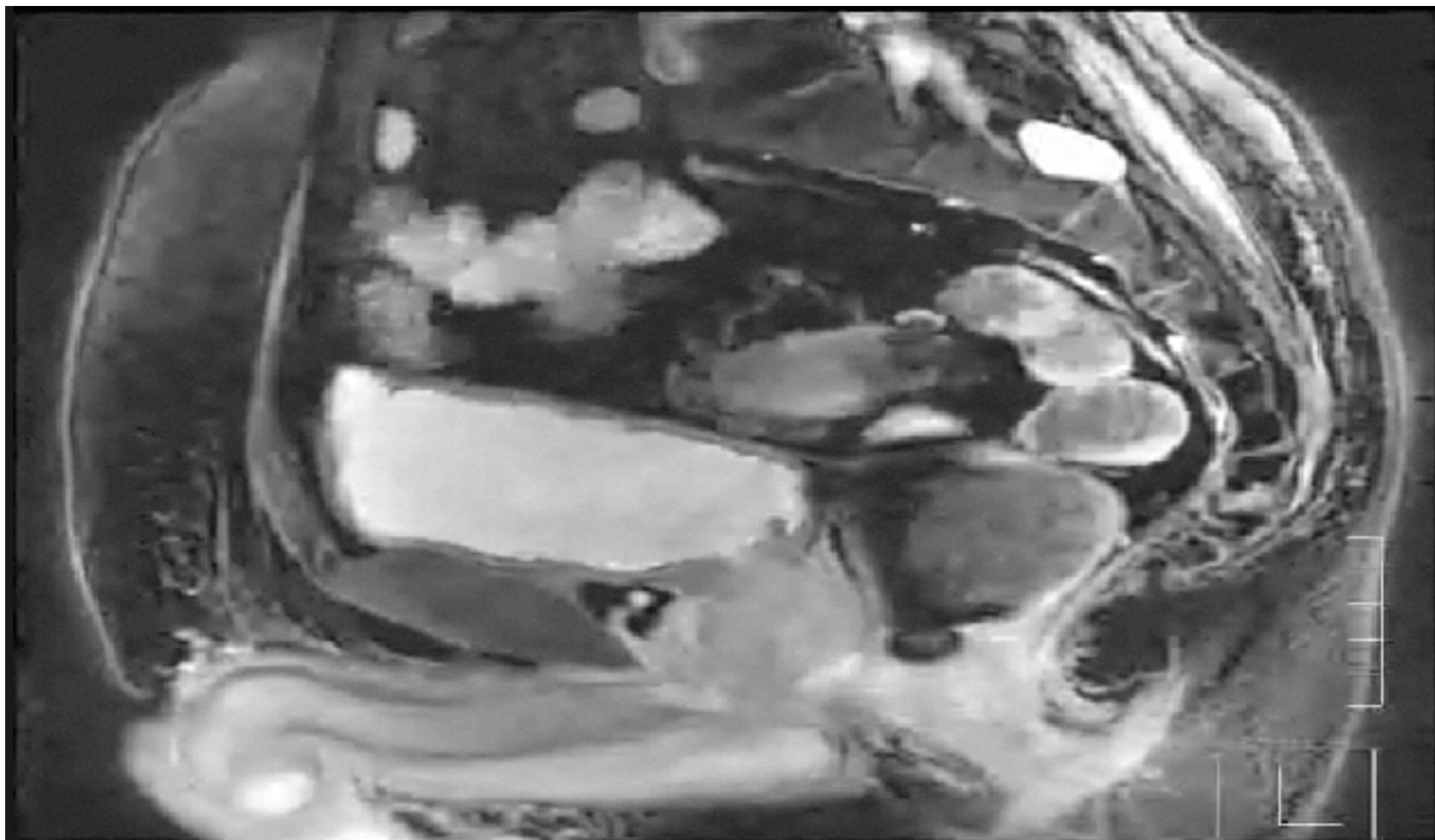
ΤΕΧΝΙΚΕΣ ΑΚΤΙΝΟΘΕΡΑΠΕΙΑΣ

Η τοποθέτηση κόκκων χρυσο στο προστάτη επιτρέπει την ακτινολογική αναγνώριση και τη διόρθωση του στόχου

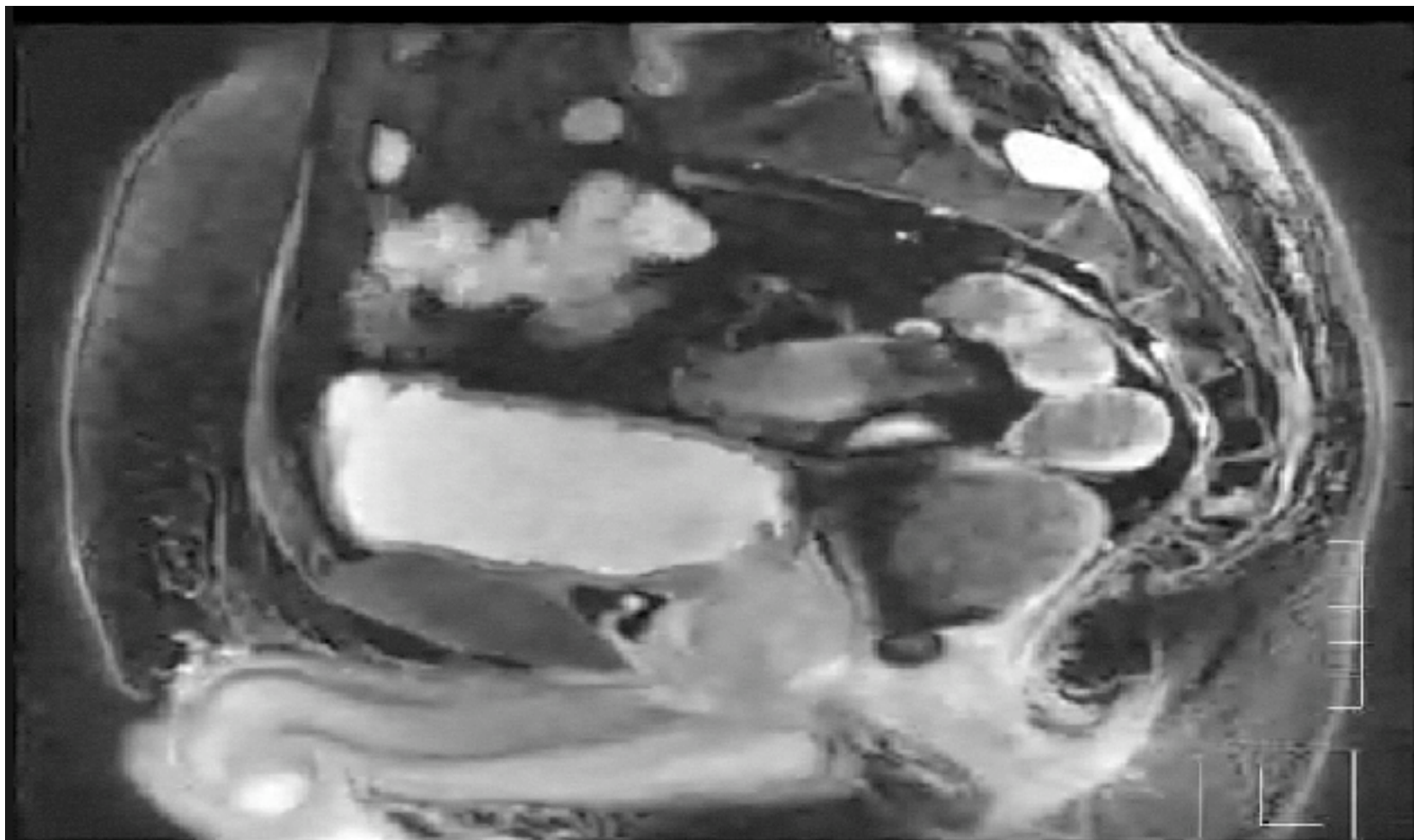
Εναλλακτικά τοποθετείται αξονικός τομογράφος μαζί με τον γραμμικό επιταχυντή για την καθημερινή επιβεβαίωση στόχου



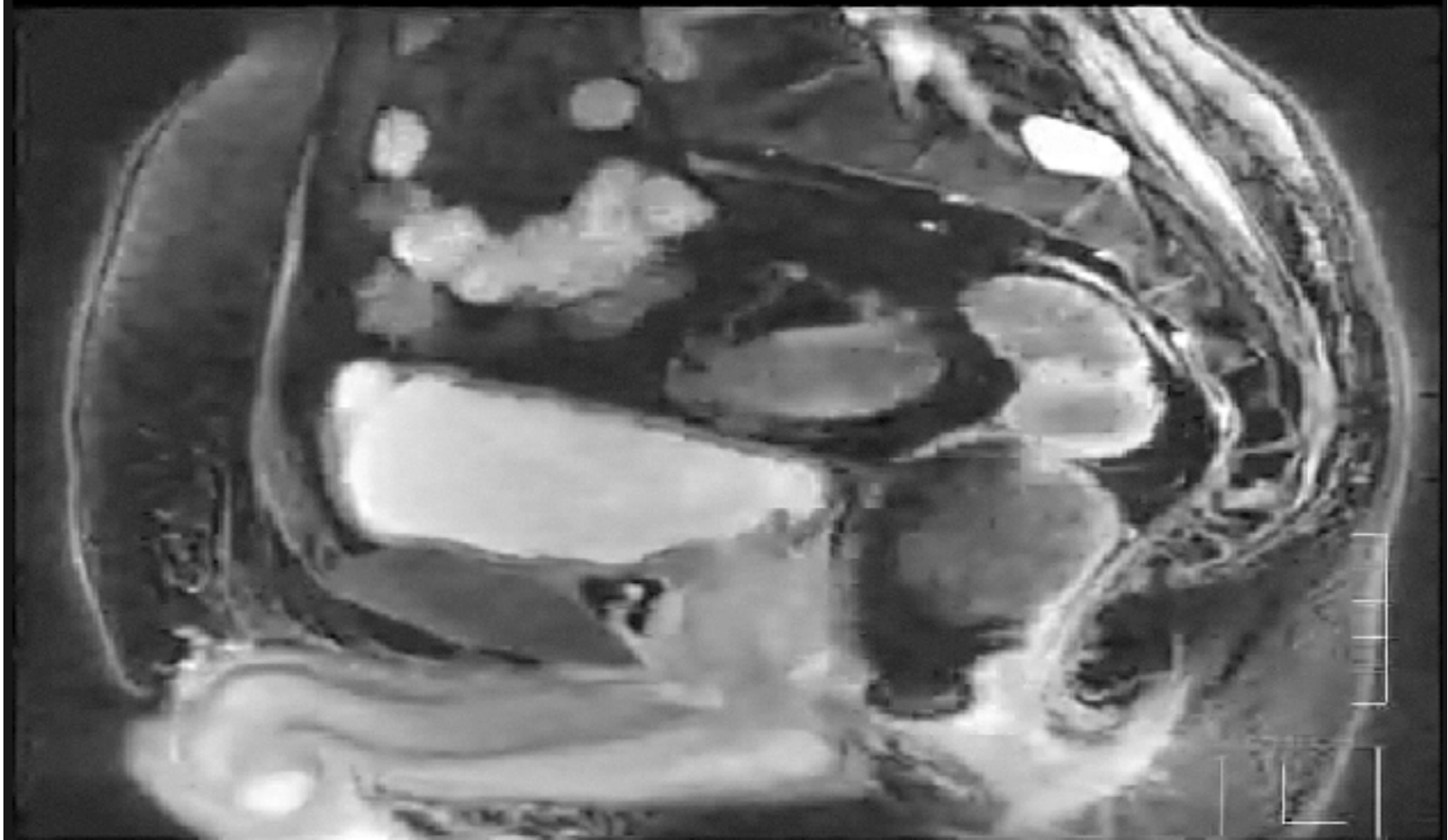
- IGRT



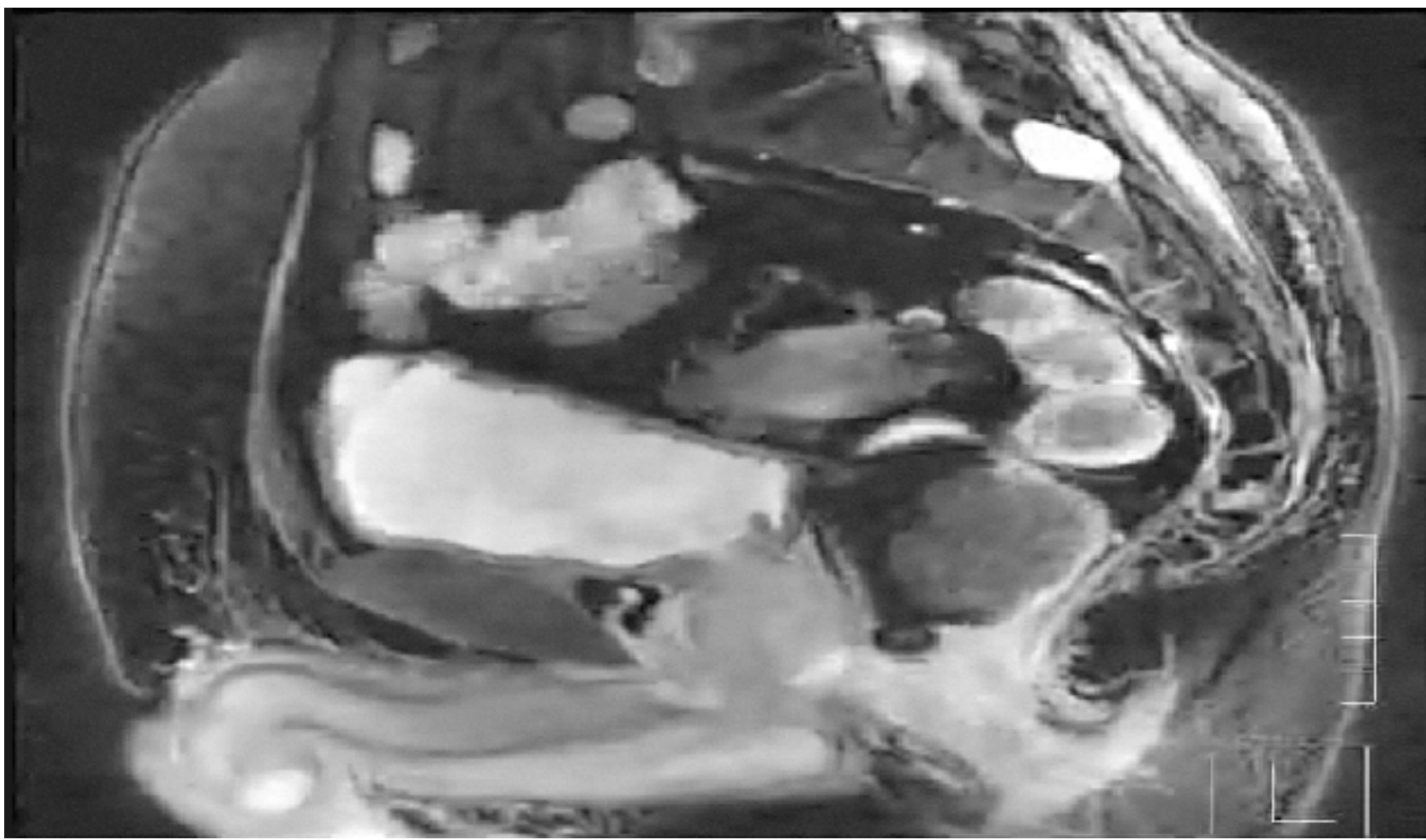
- IGRT



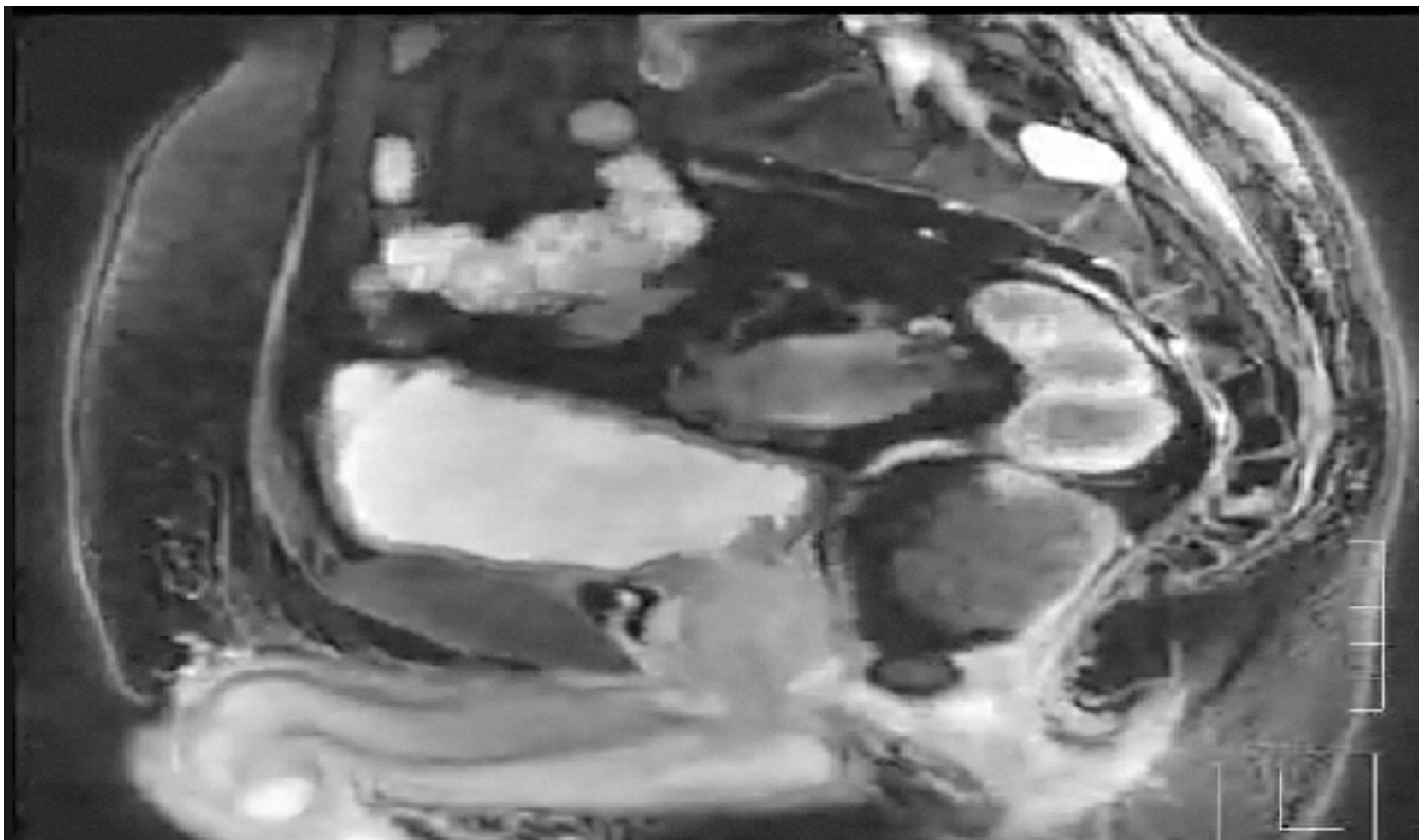
- IGRT



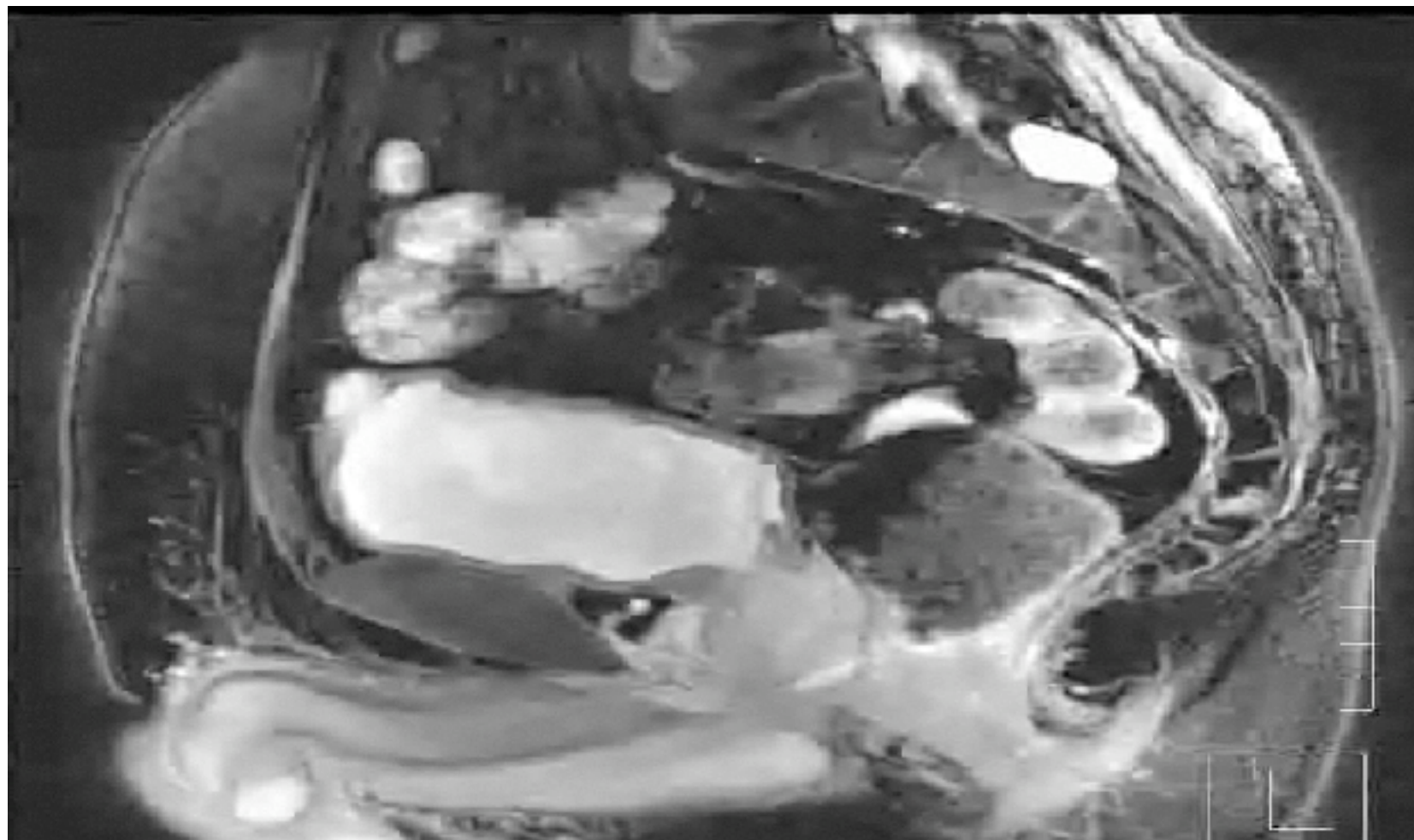
- IGRT



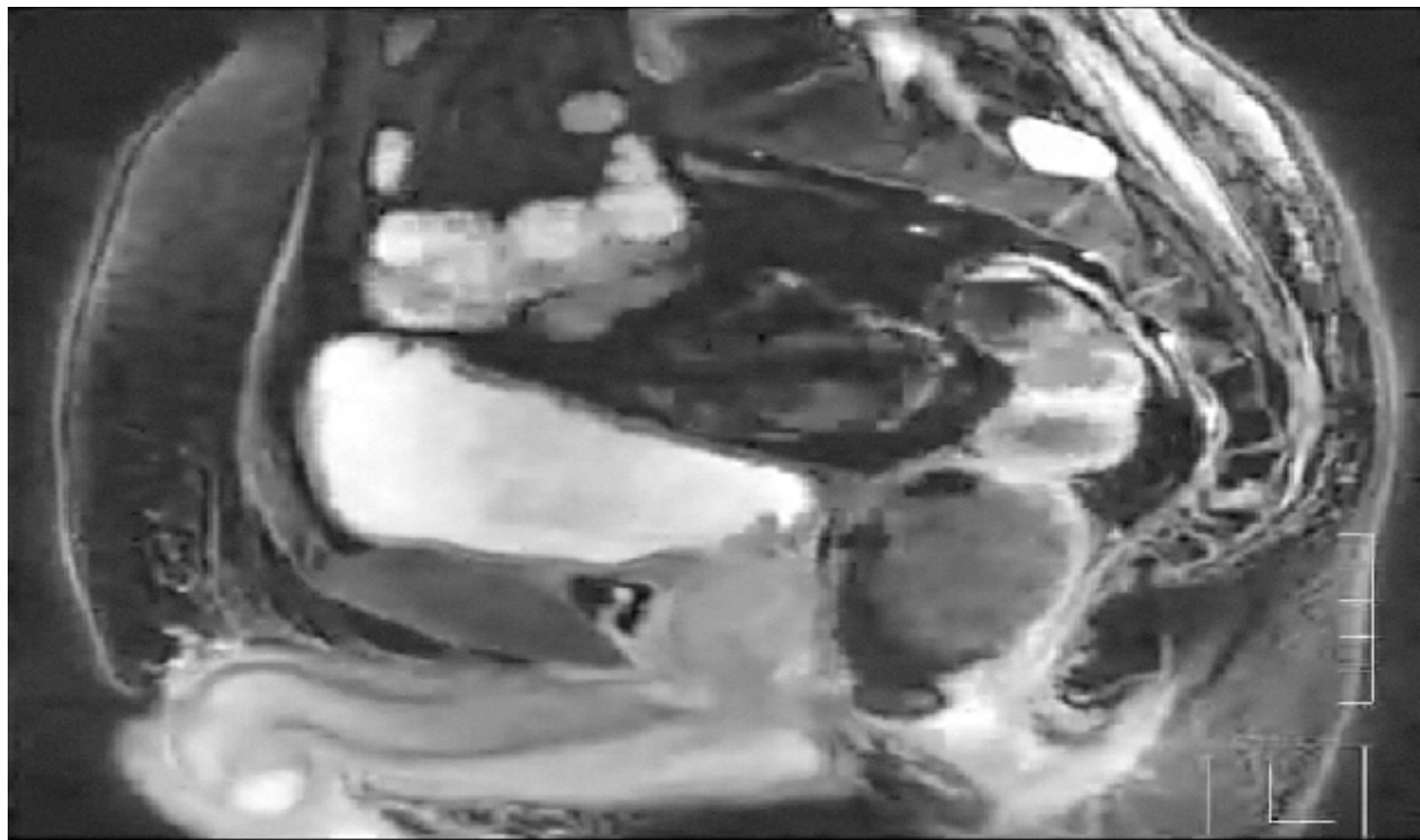
- IGRT



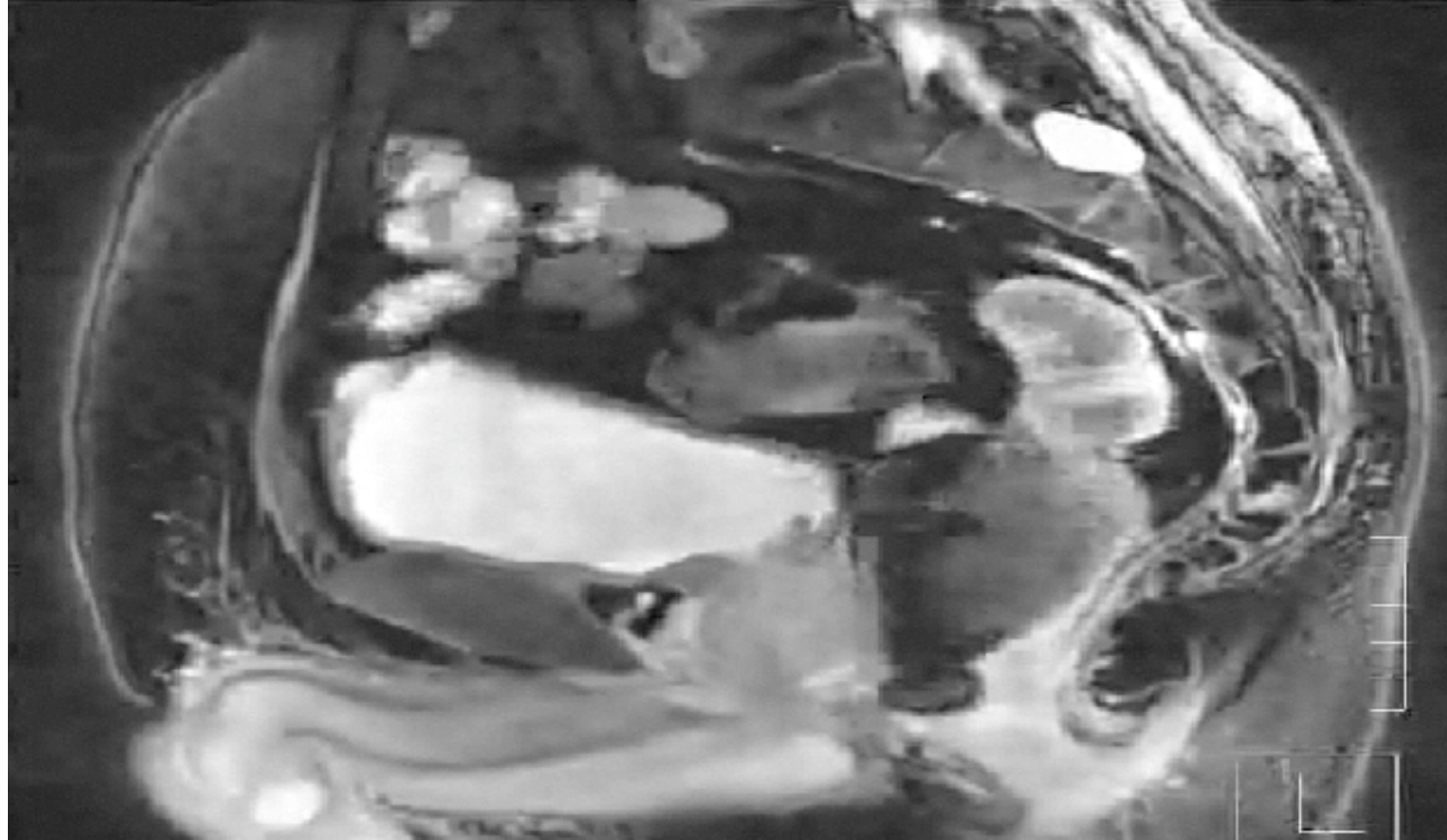
- IGRT



- IGRT



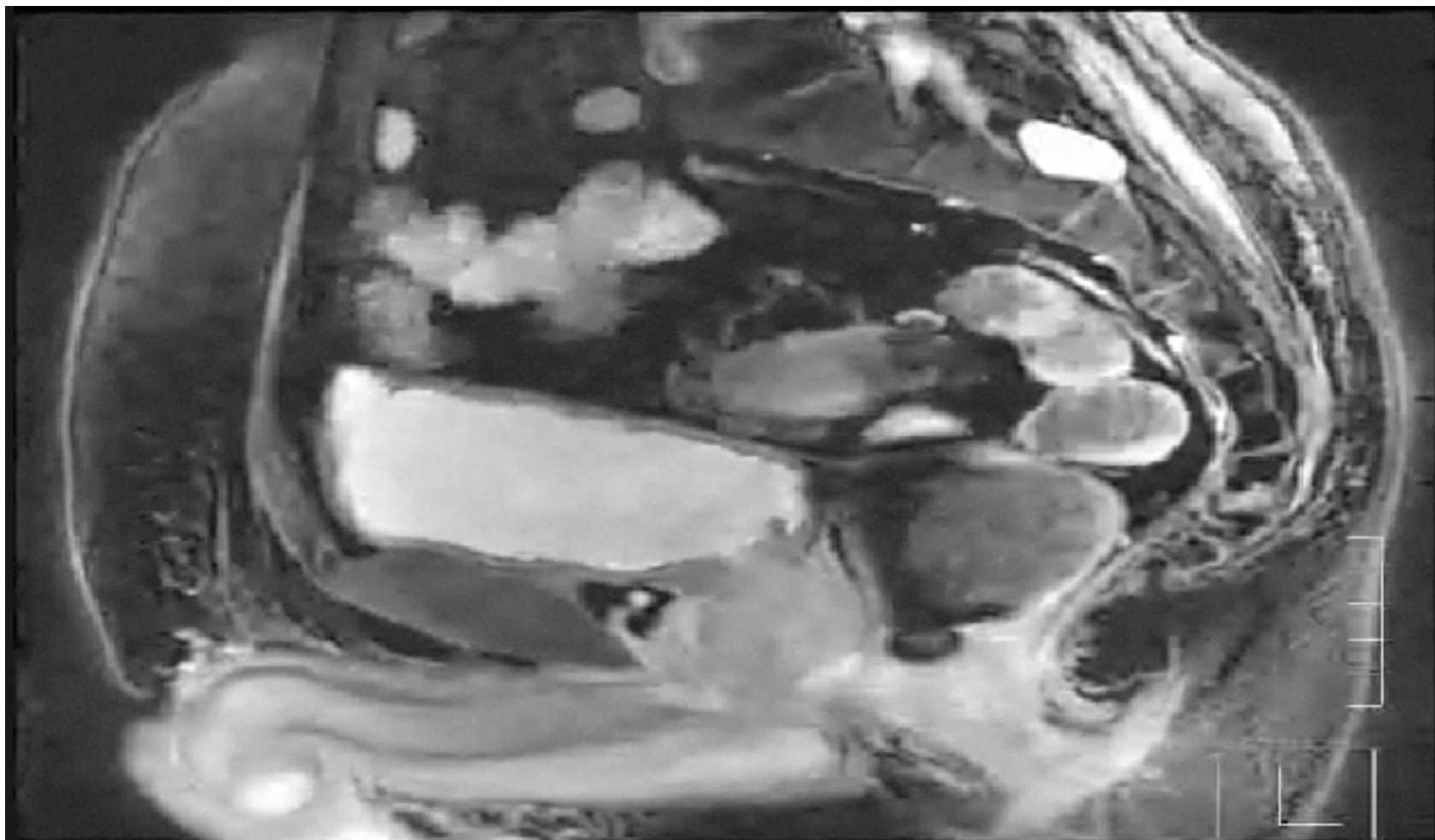
- IGRT



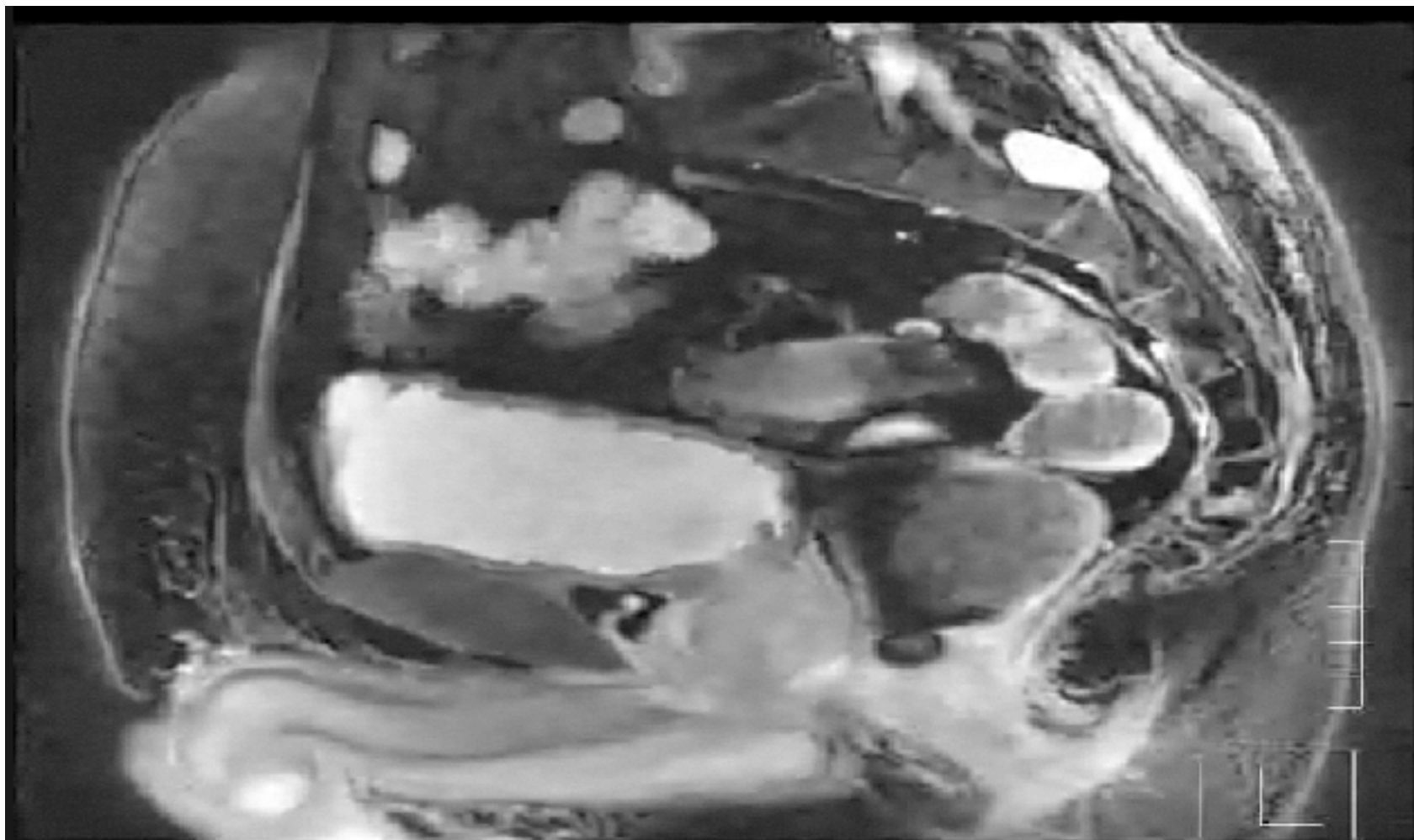
- IGRT



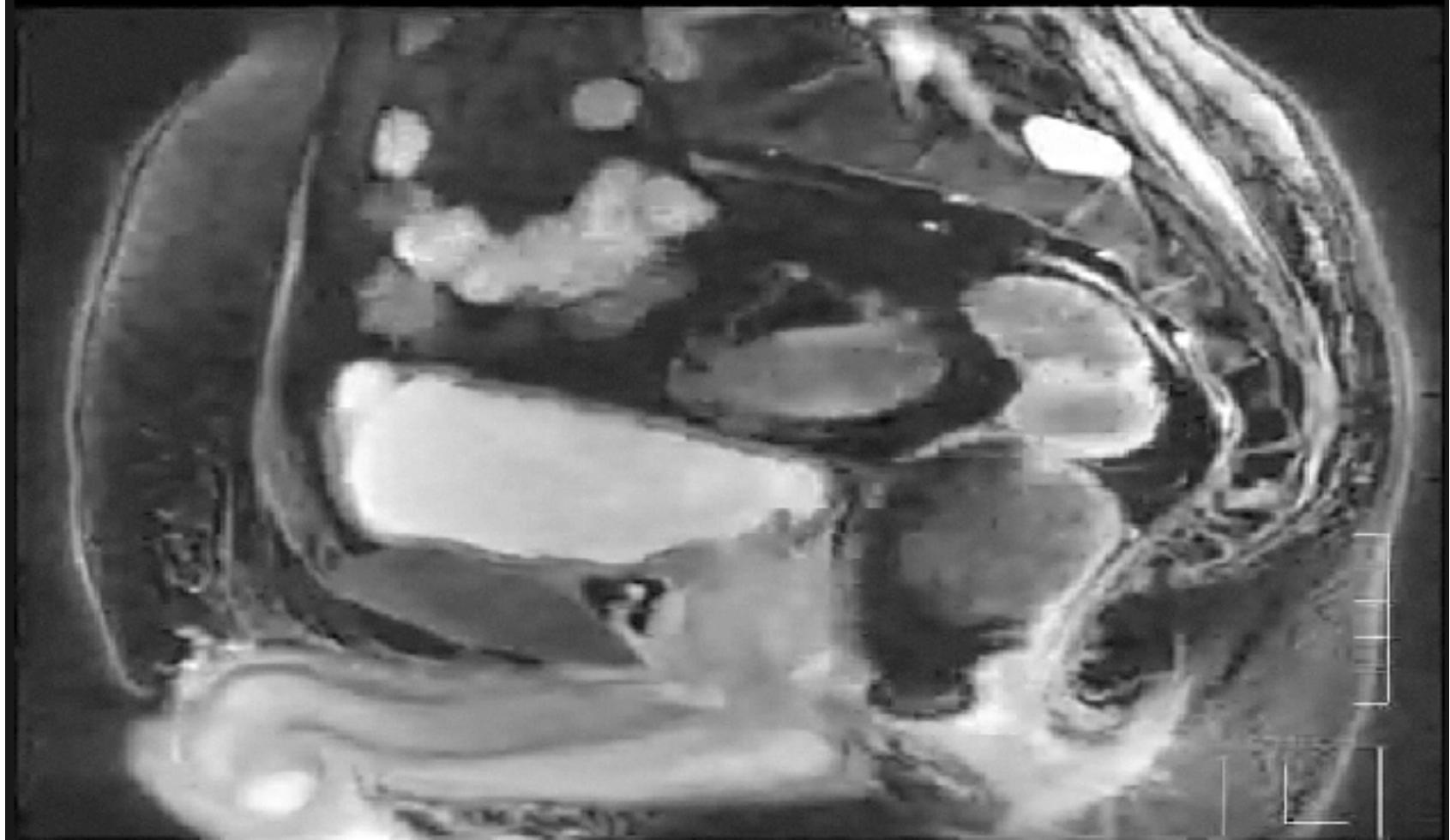
- IGRT



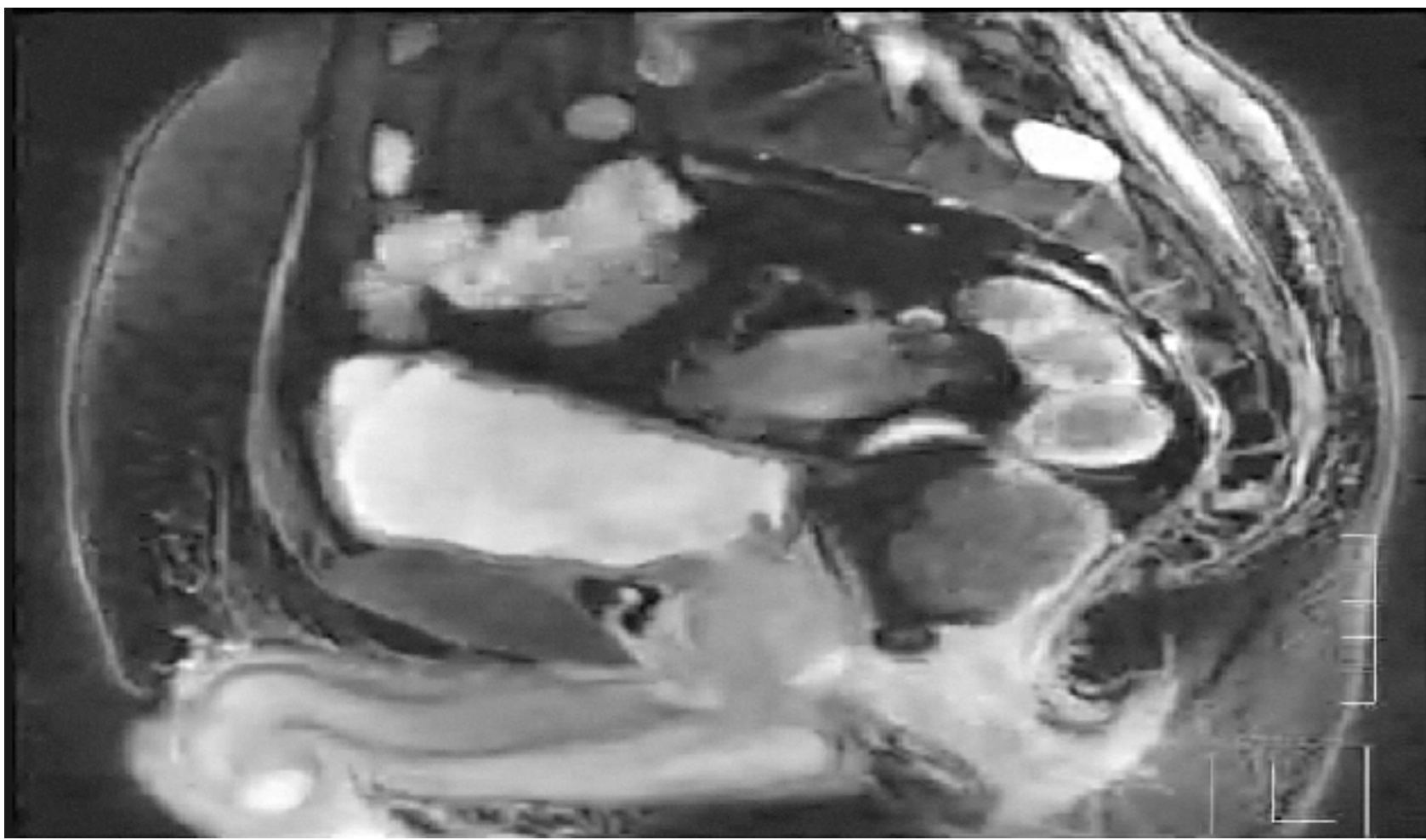
- IGRT



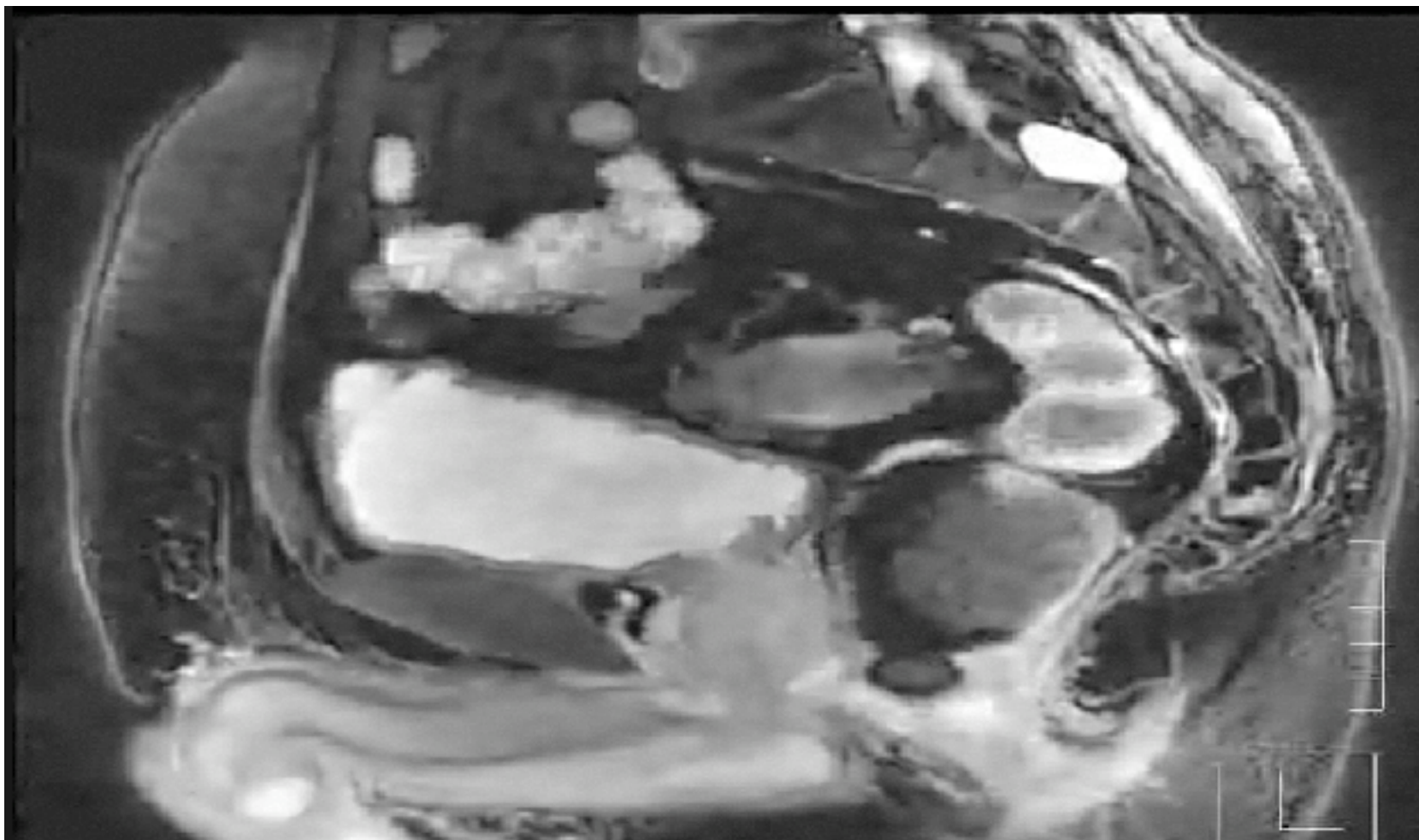
- IGRT



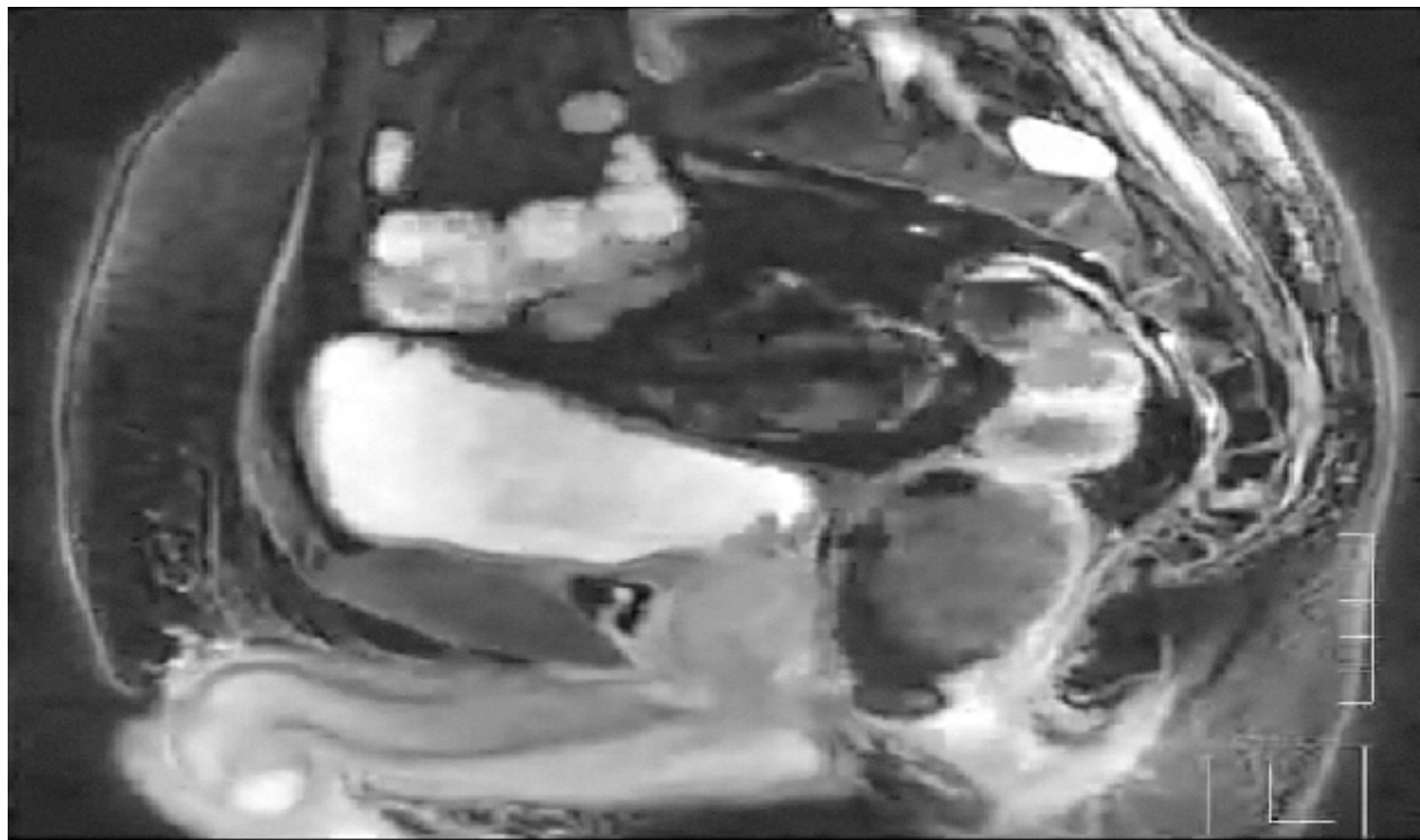
- IGRT



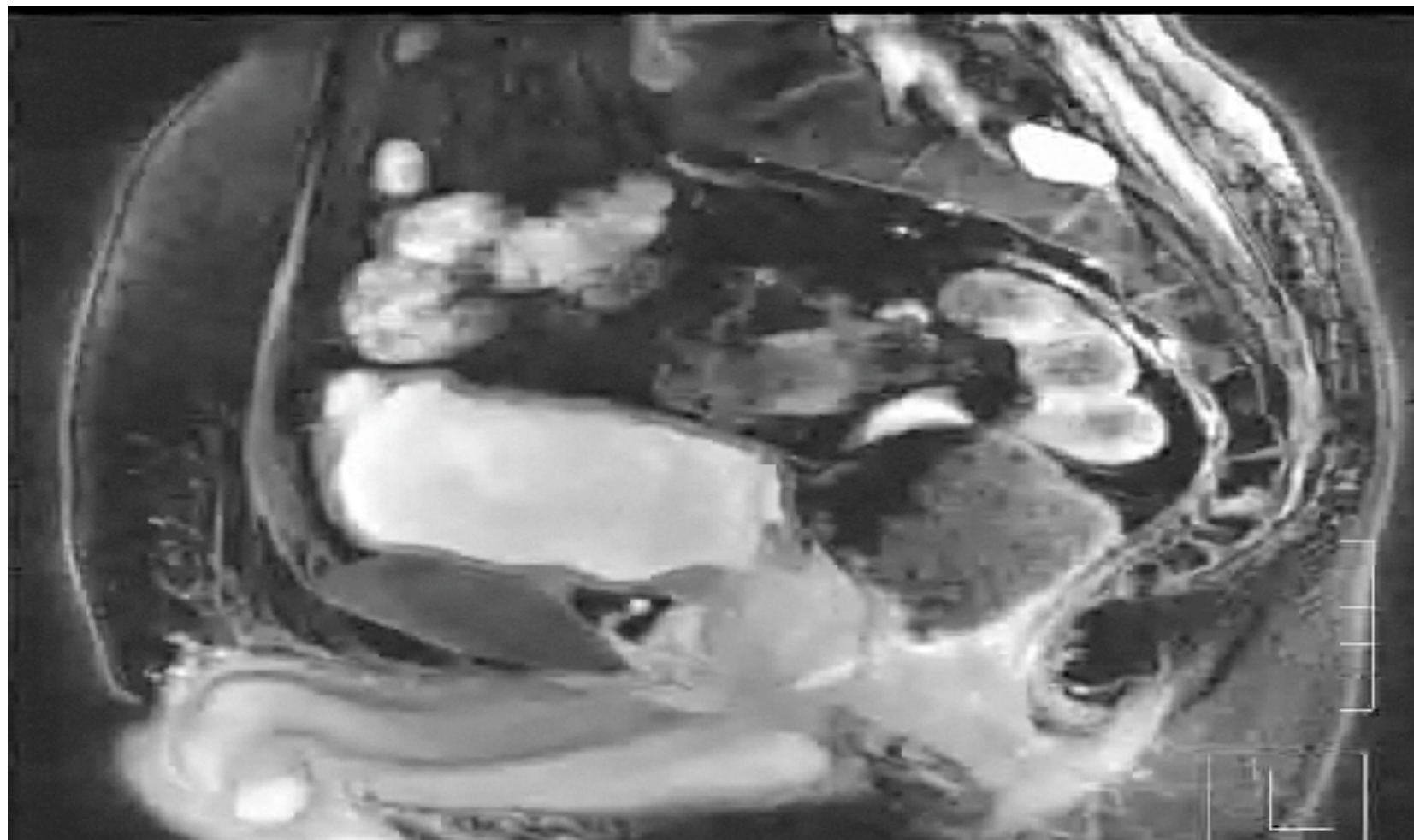
- IGRT



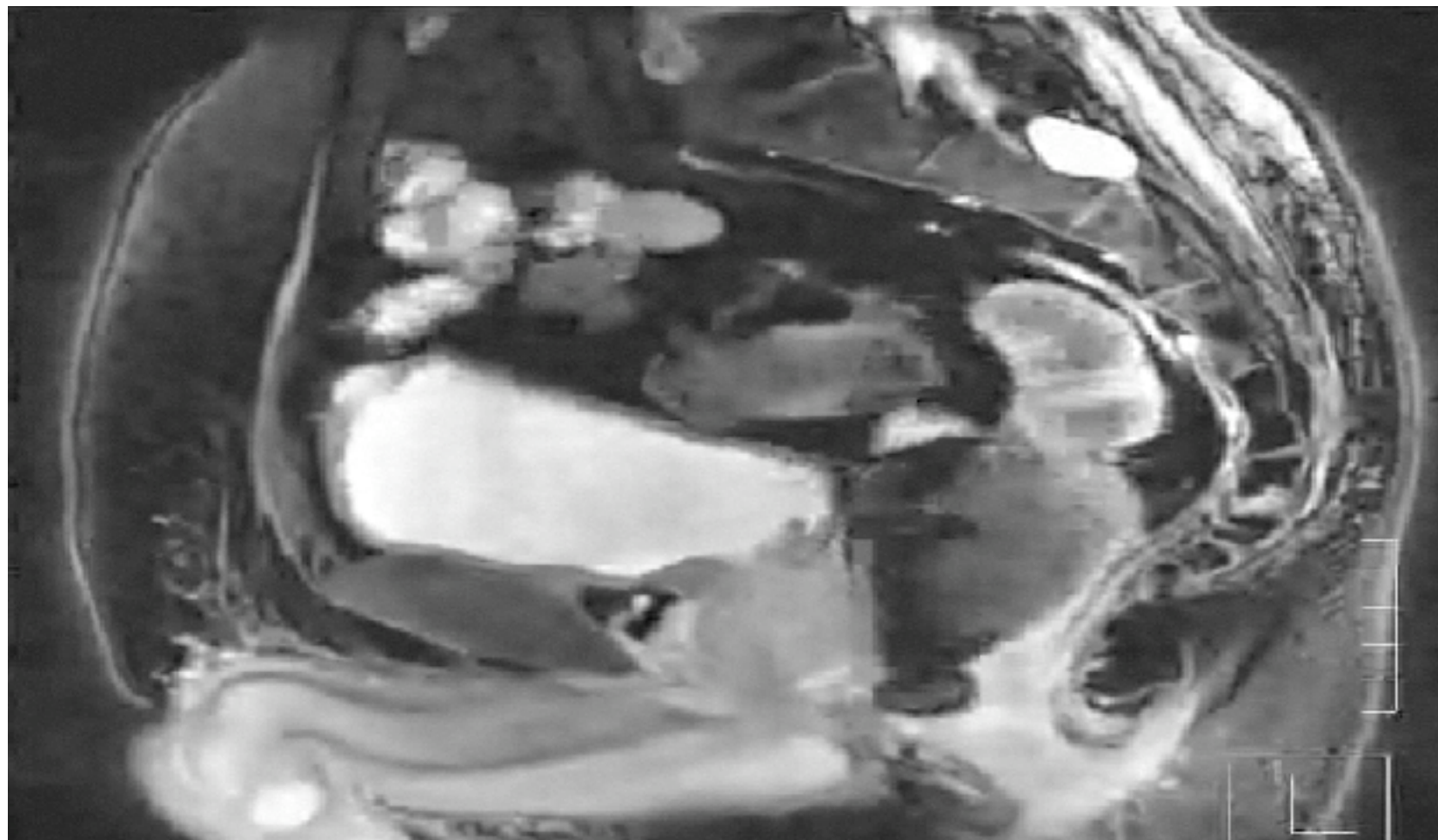
- IGRT



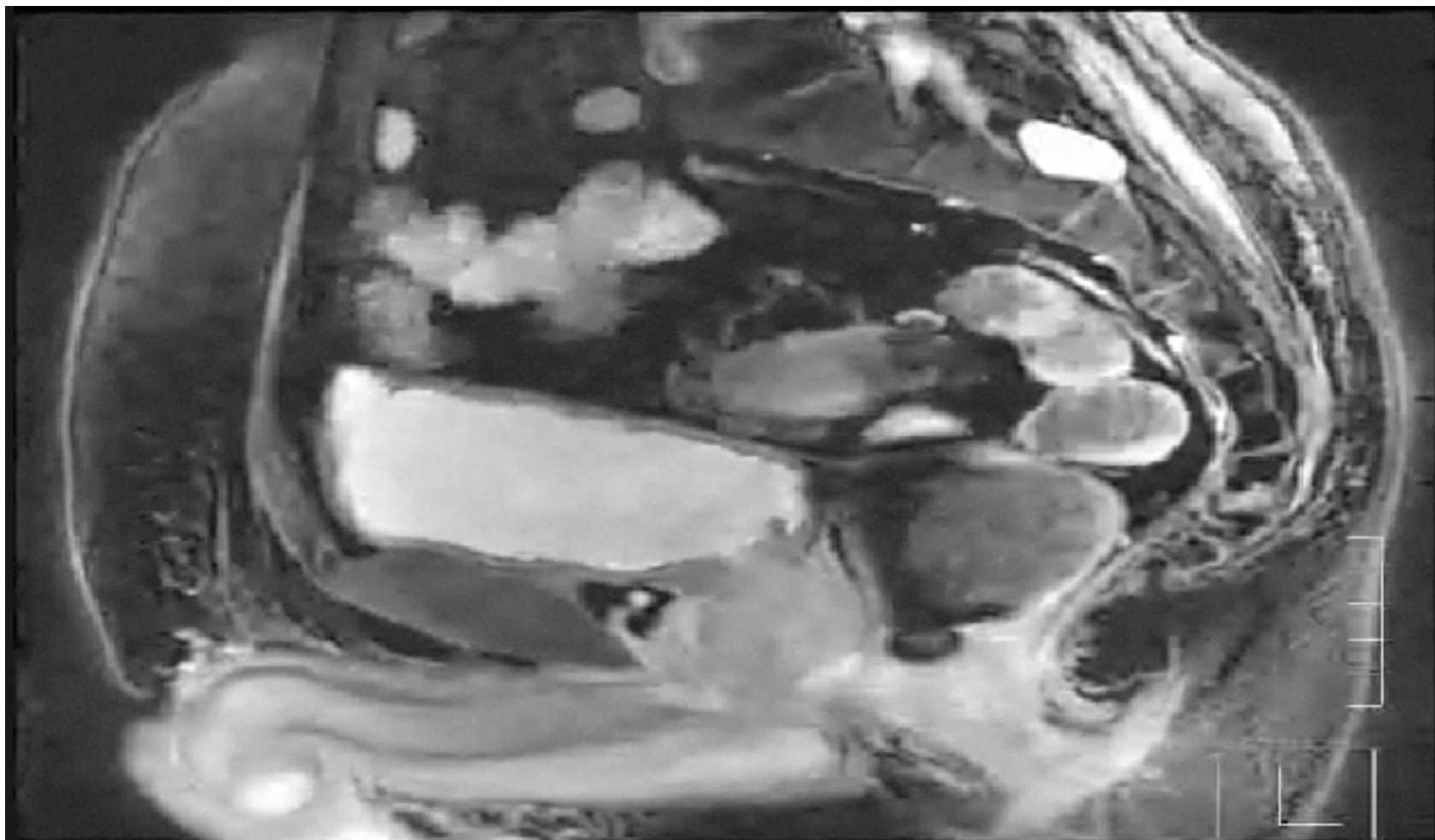
- IGRT



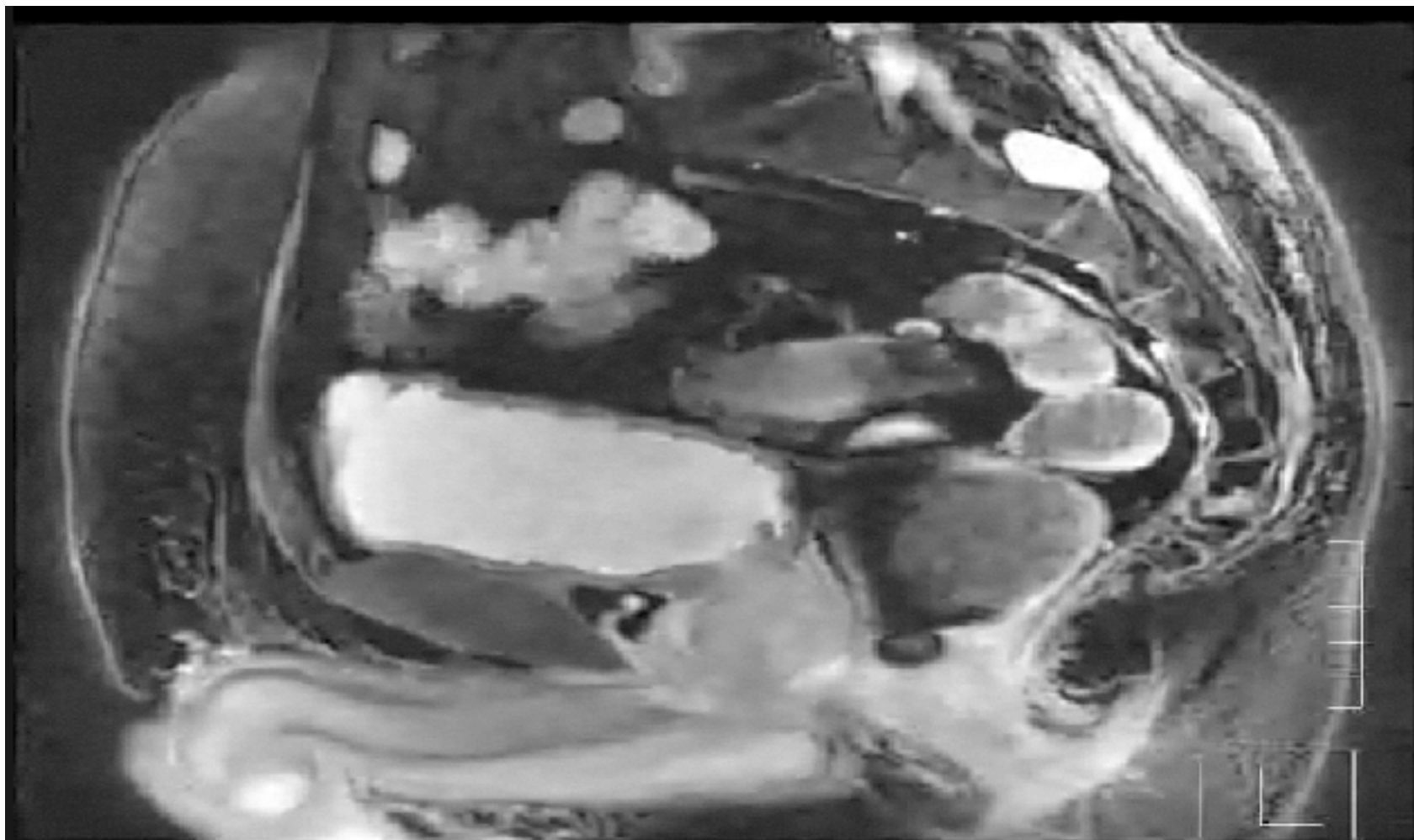
- IGRT



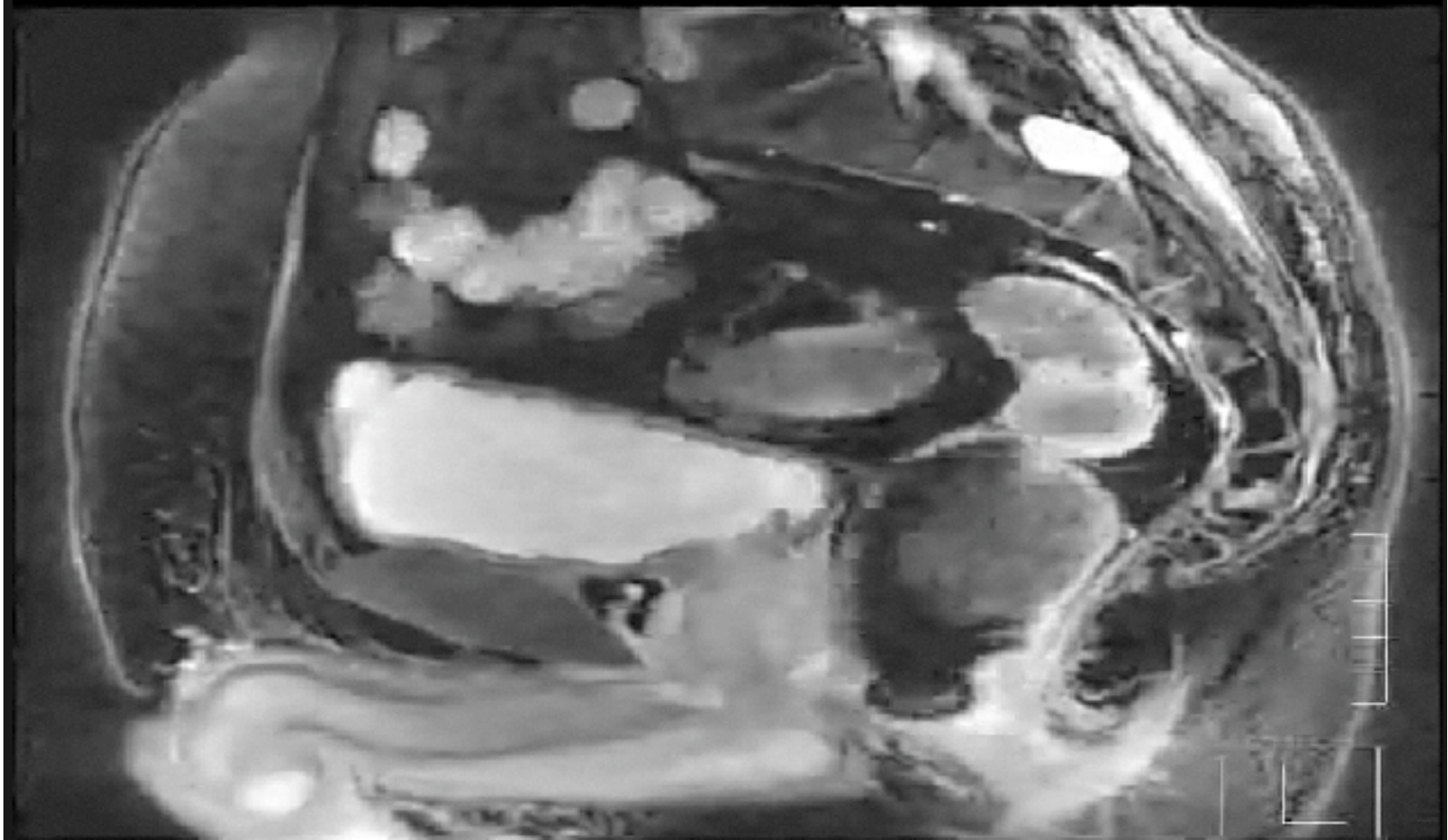
- IGRT



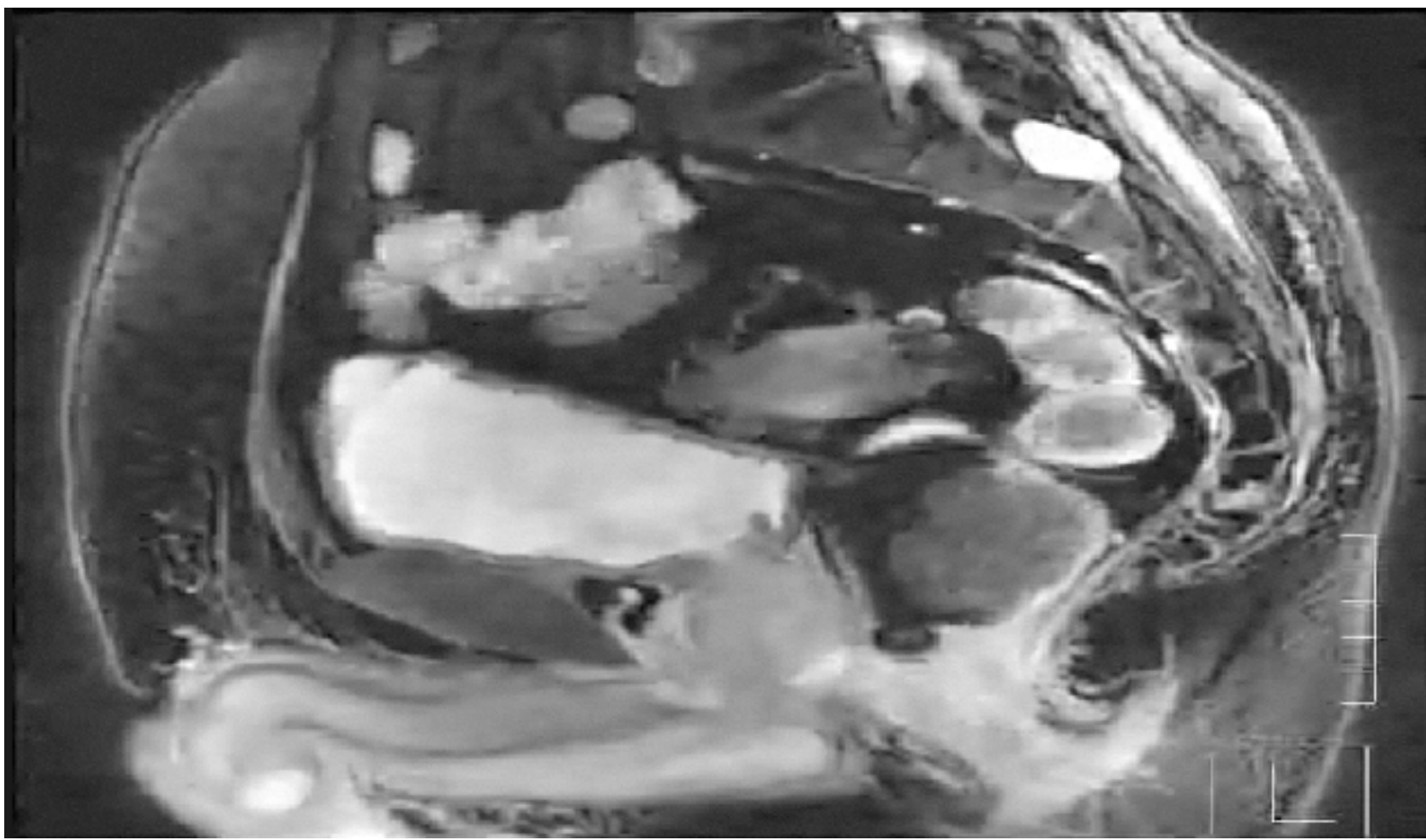
- IGRT



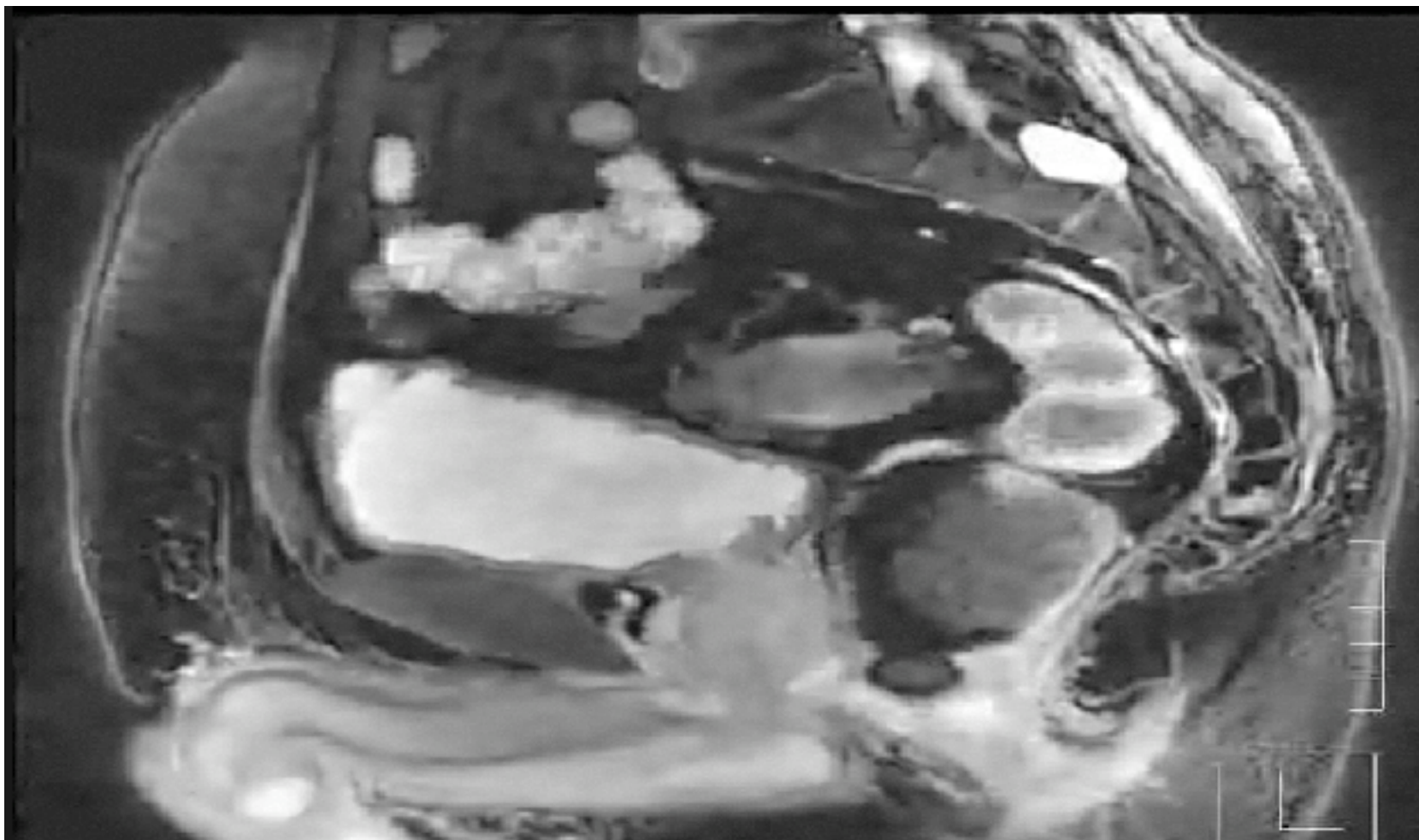
- IGRT



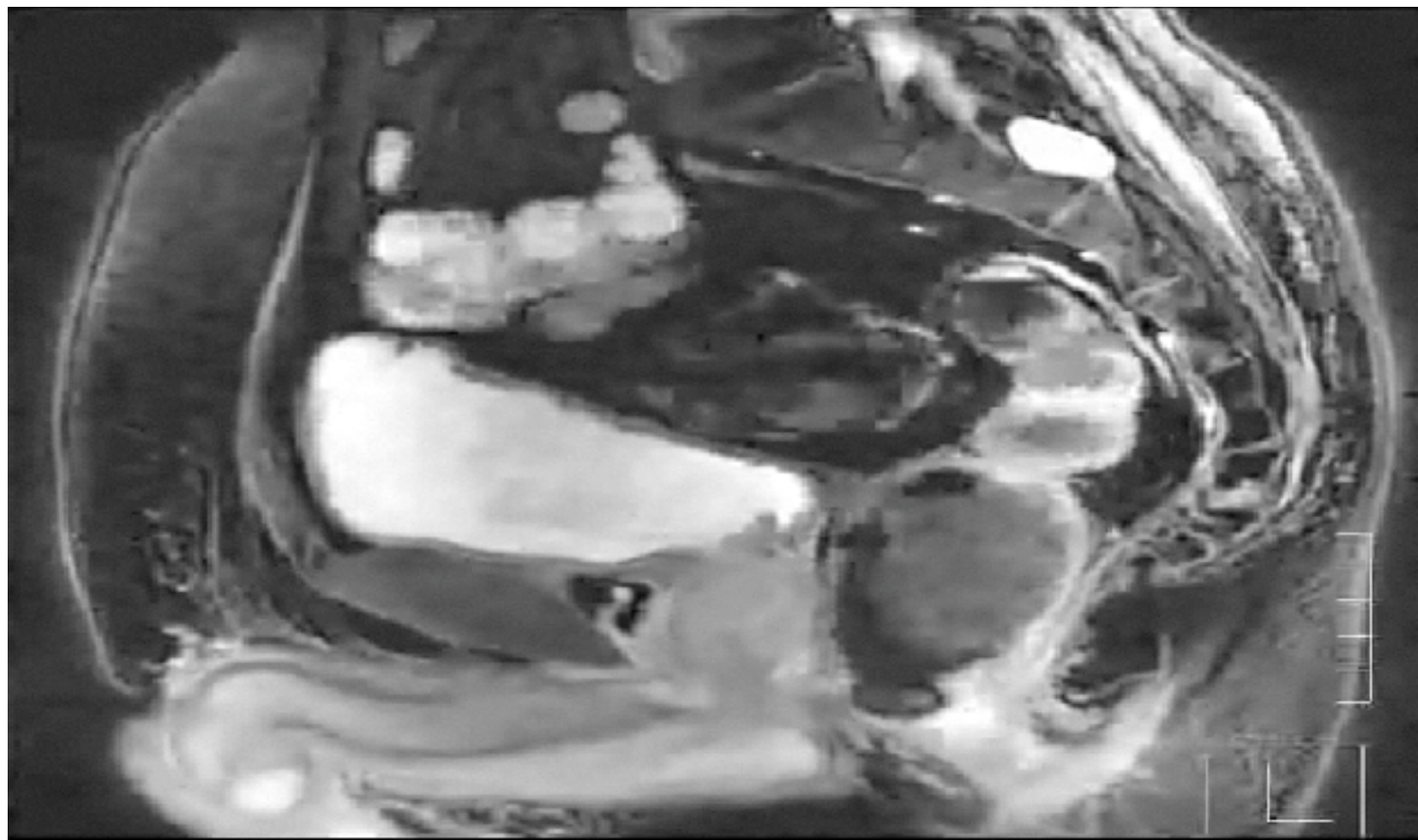
- IGRT



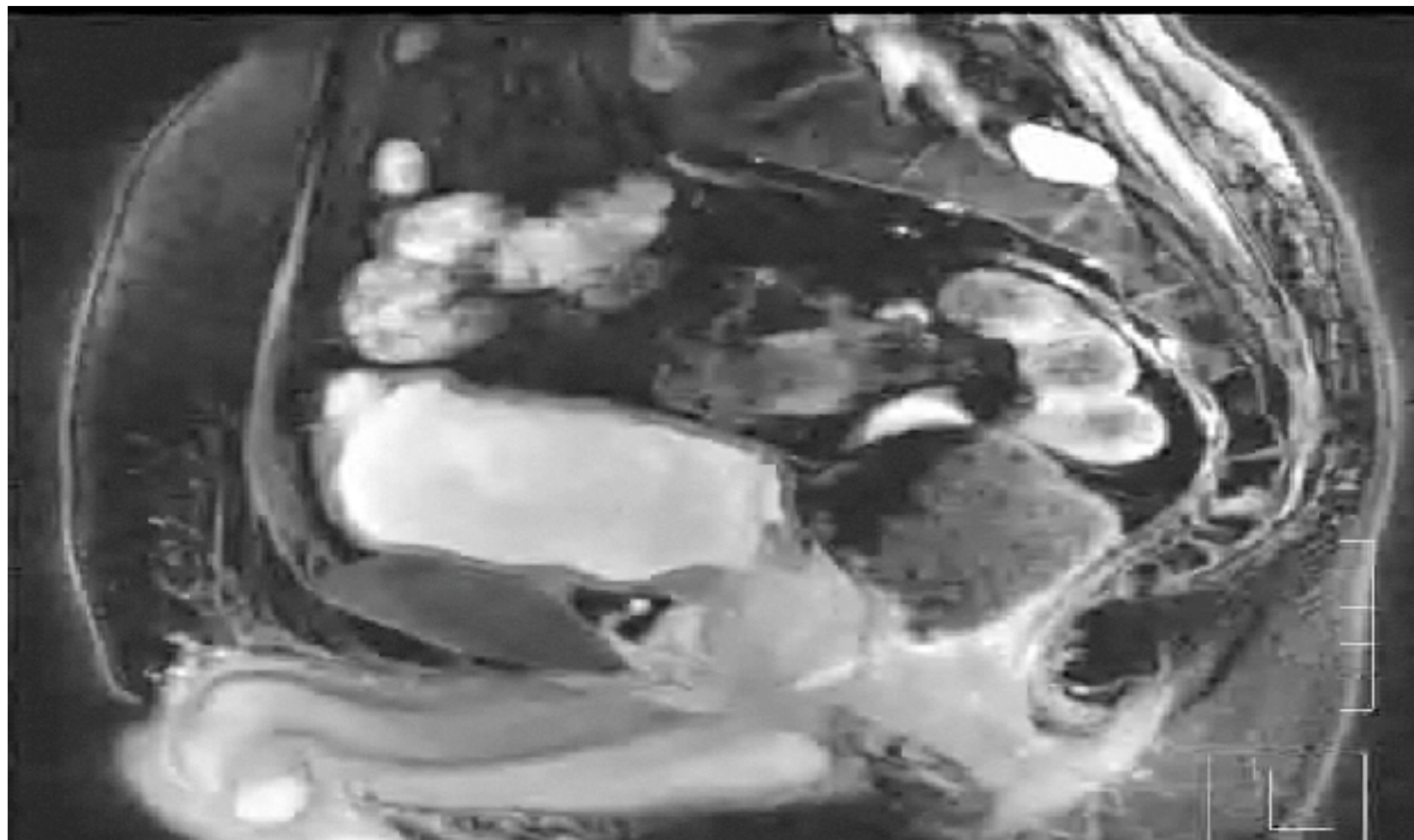
- IGRT



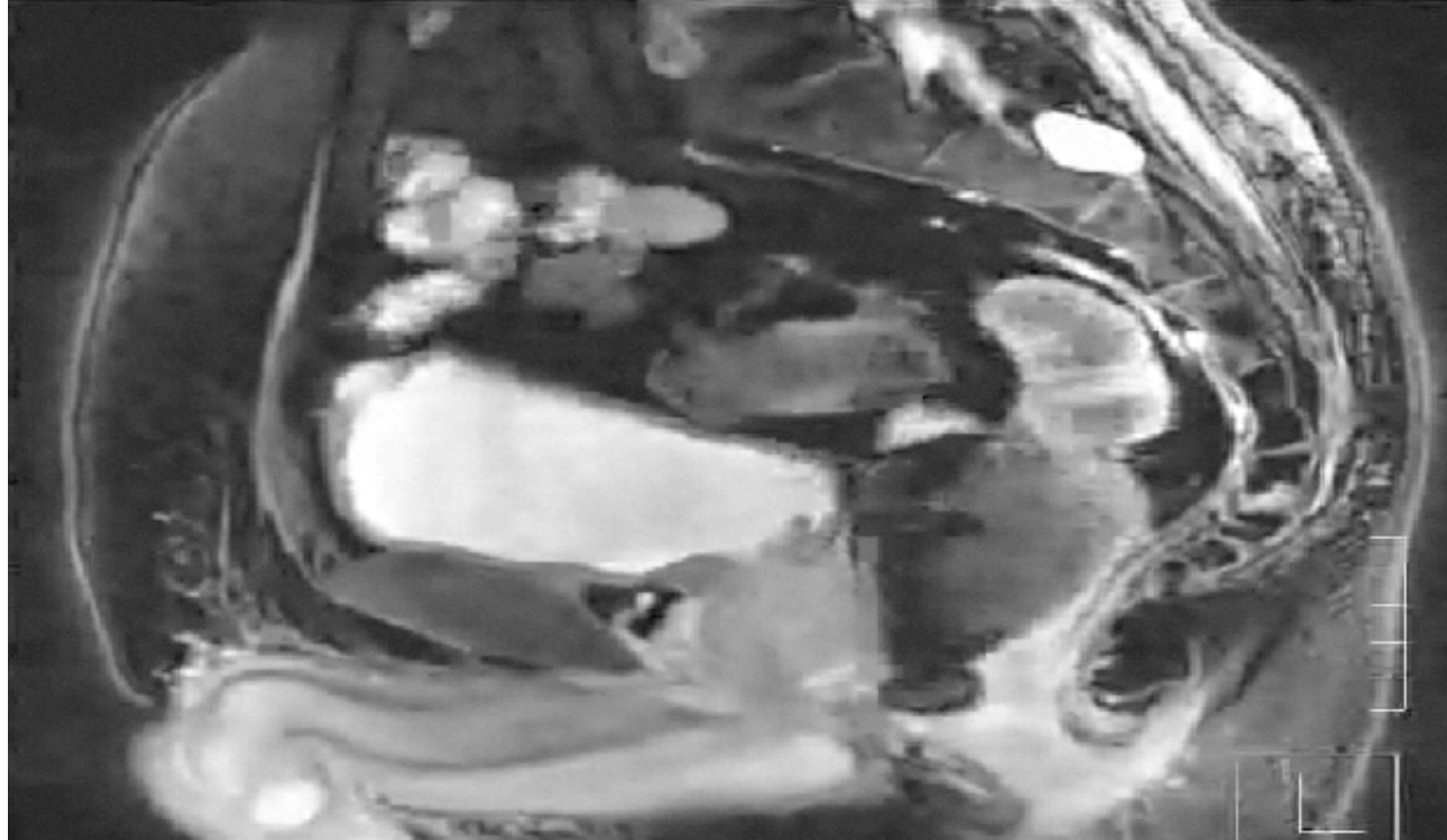
- IGRT

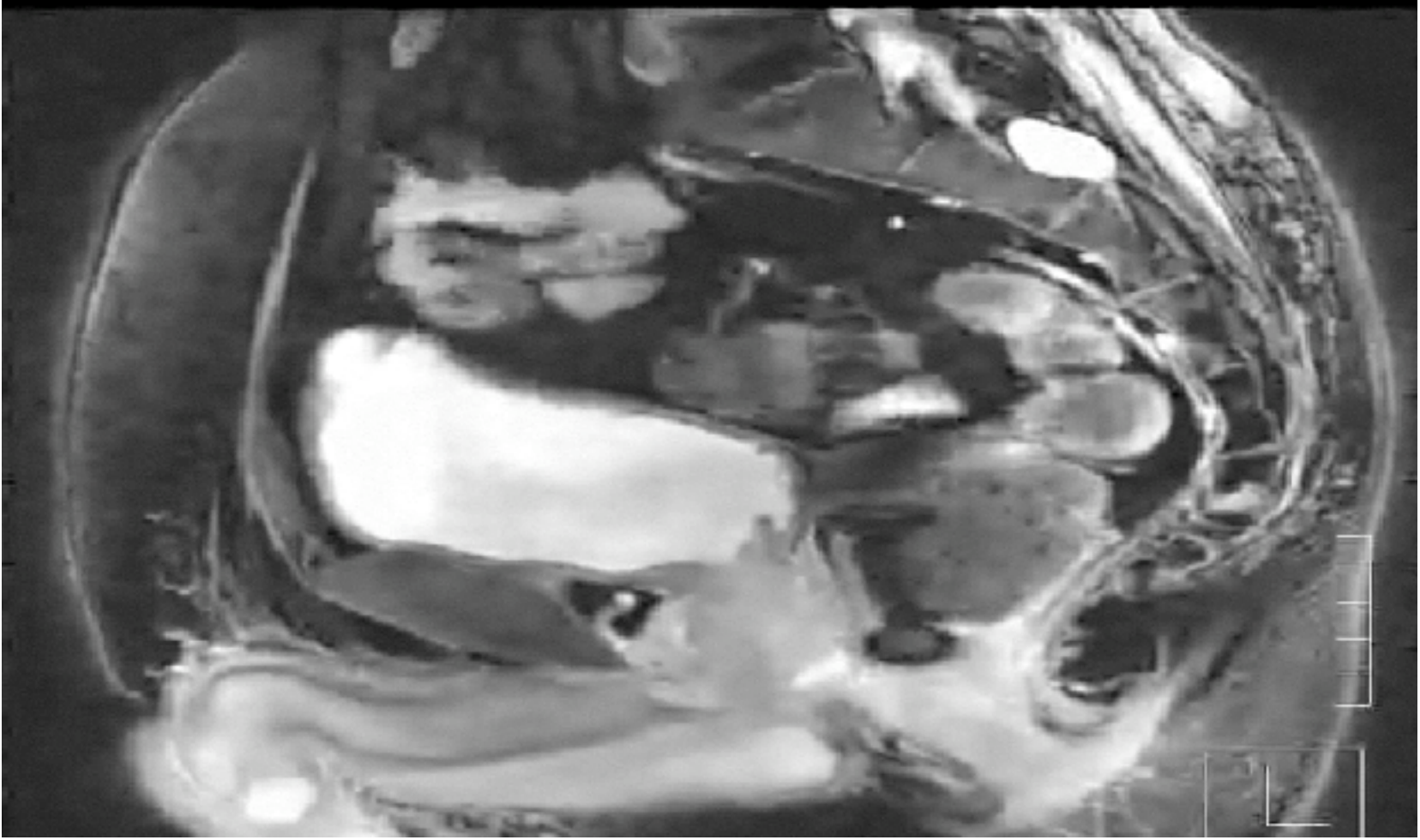


- IGRT

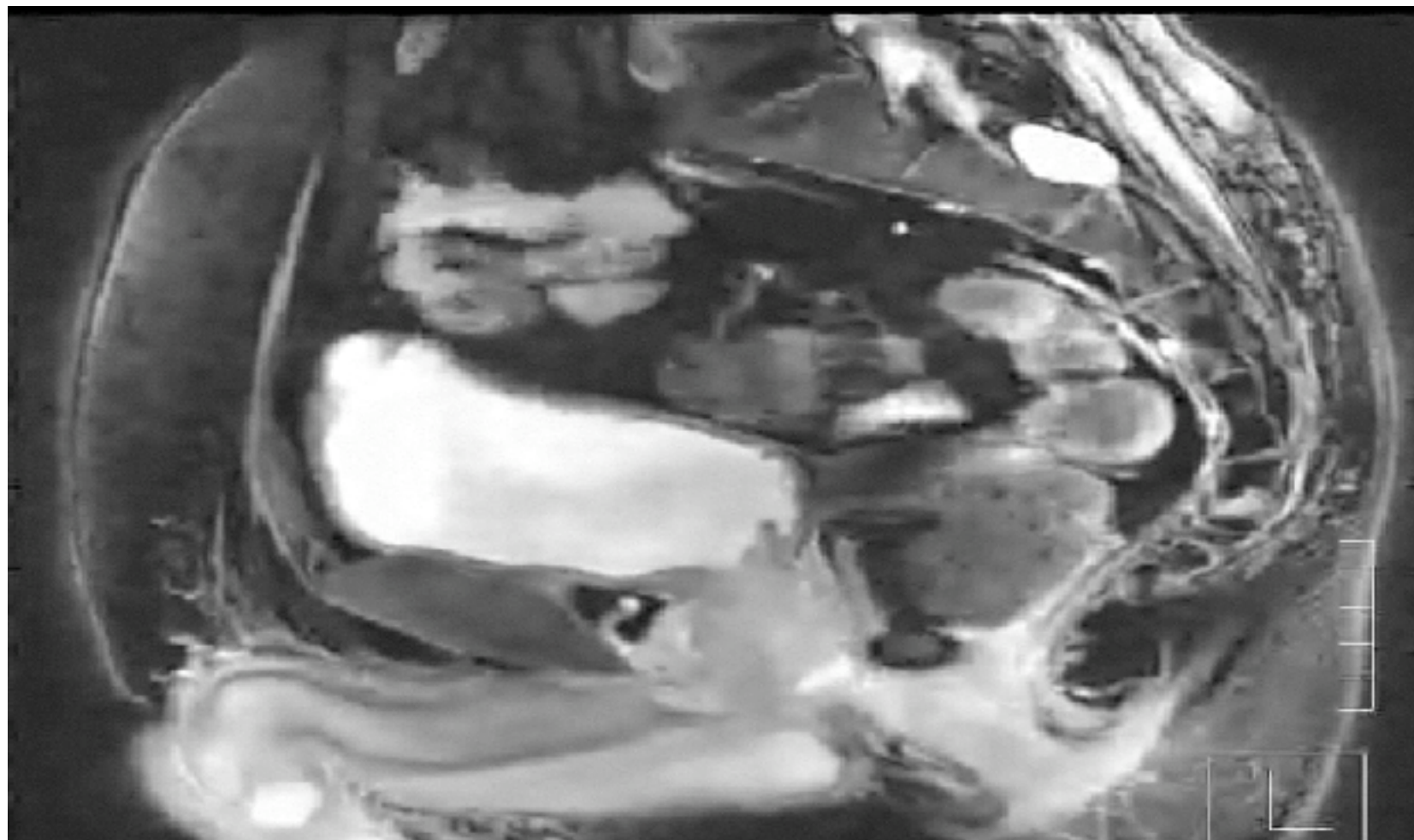


- IGRT

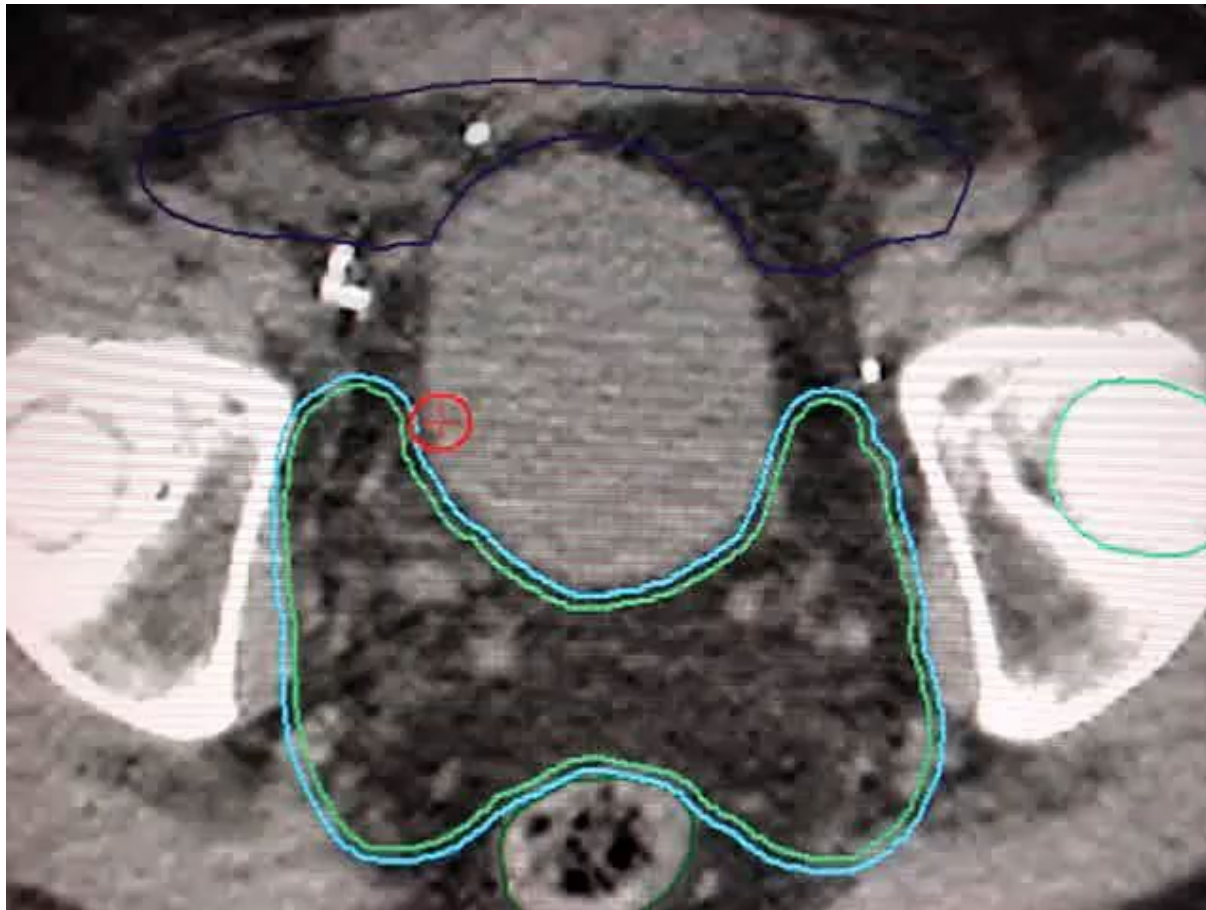




- IGRT



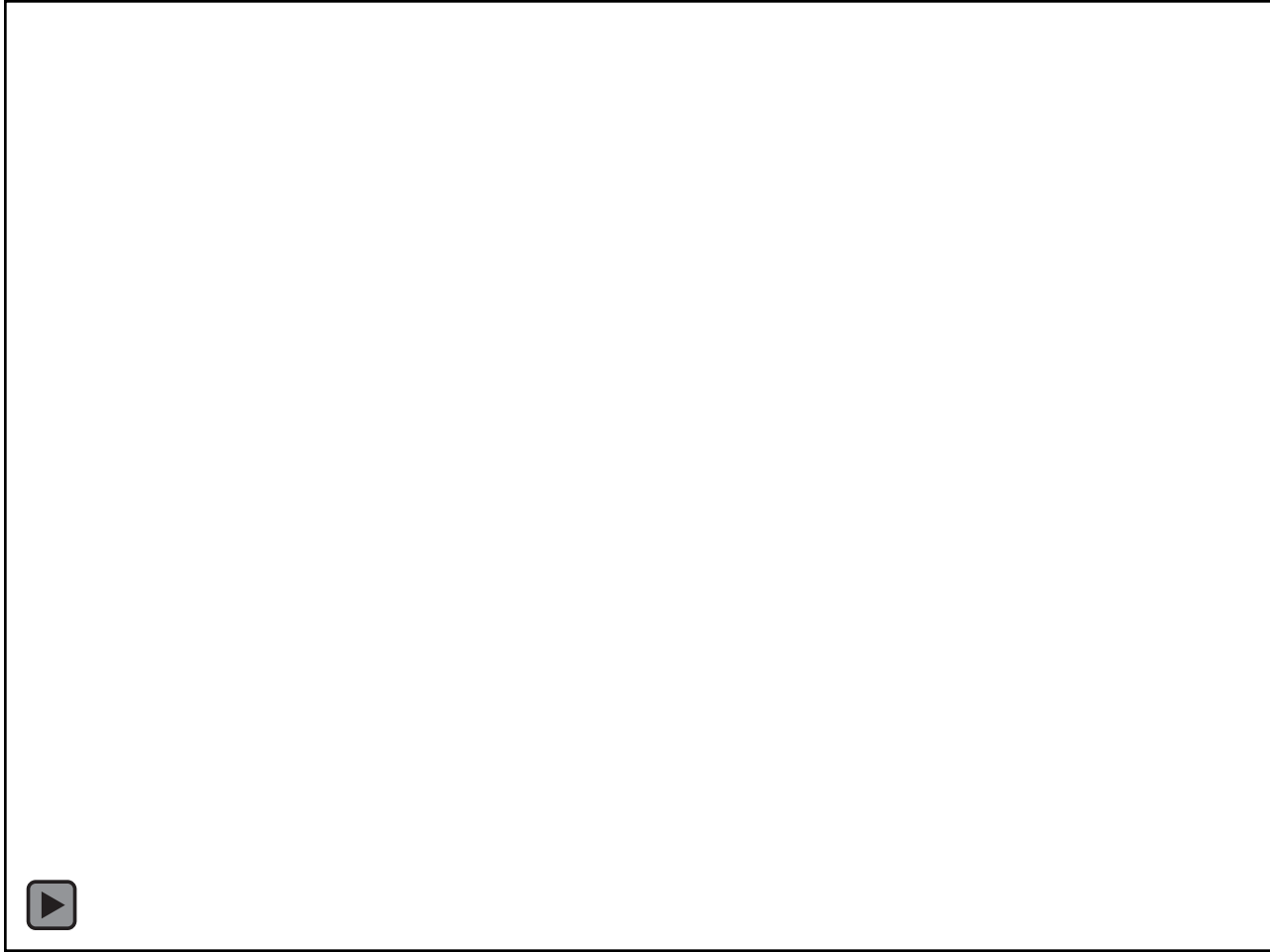
- Σχεδιασμός στόχων και προστατευόμενων οργάνων



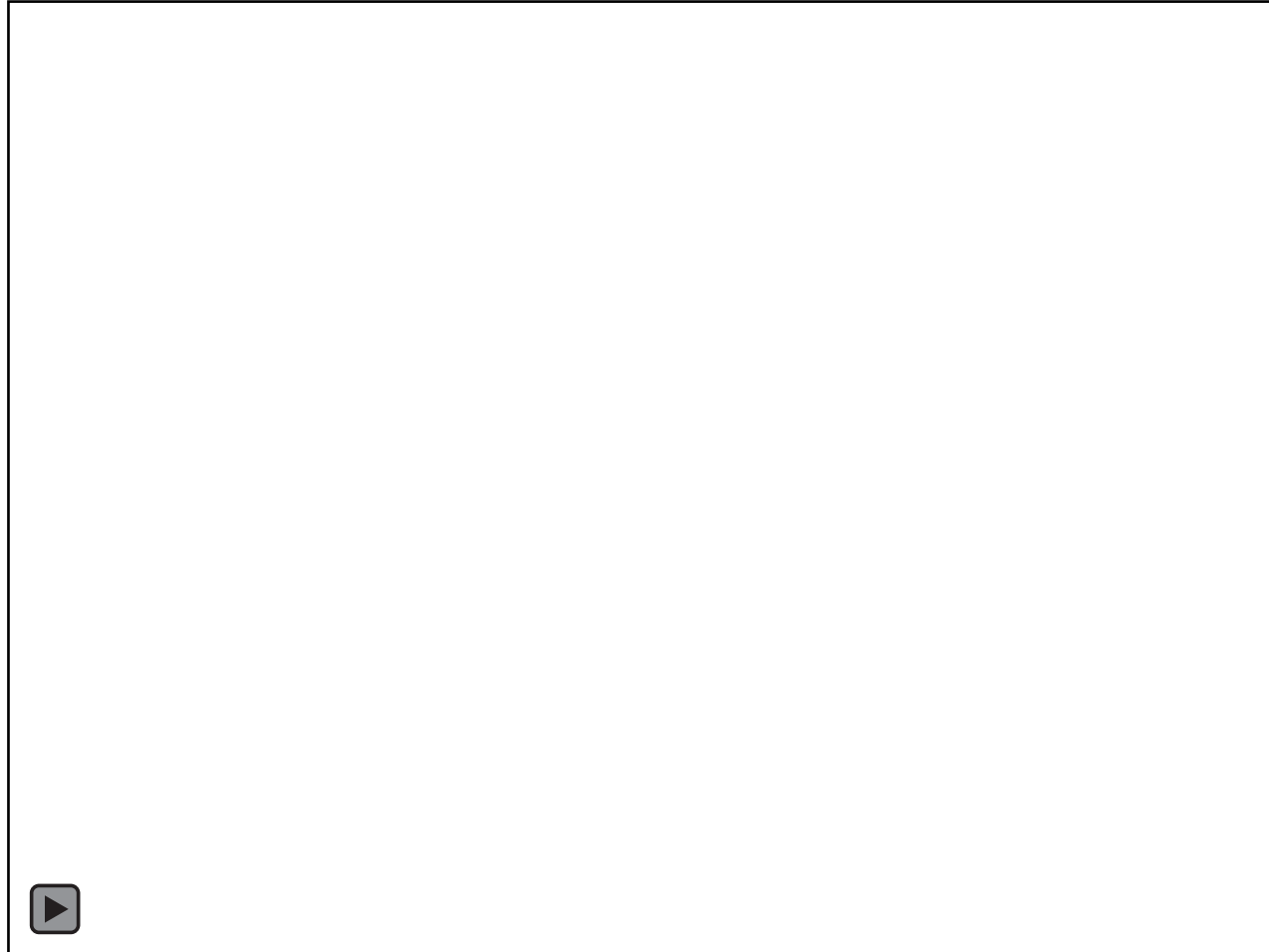
- Στερεοσκοπική εμφάνιση στόχων, OAR

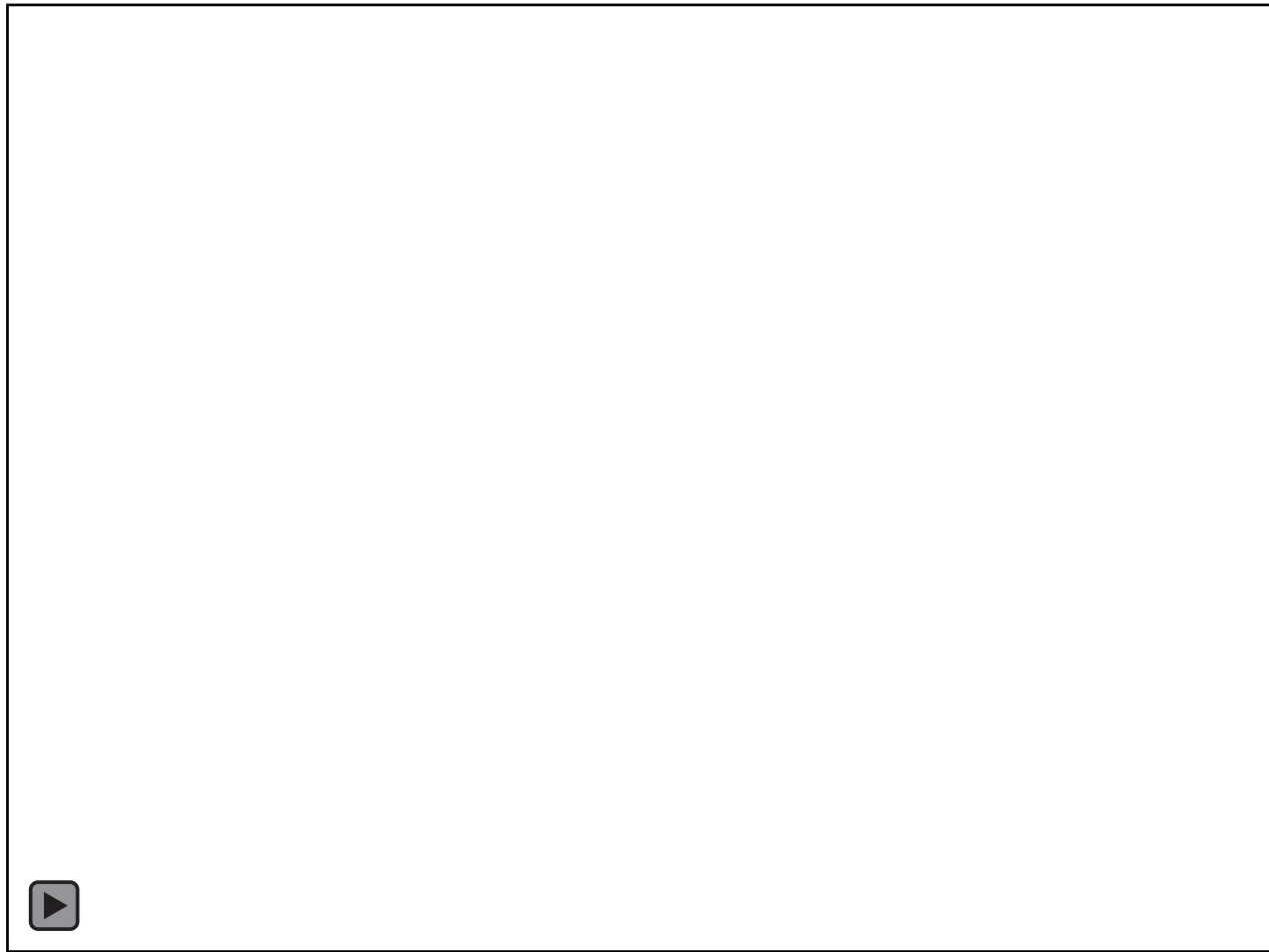


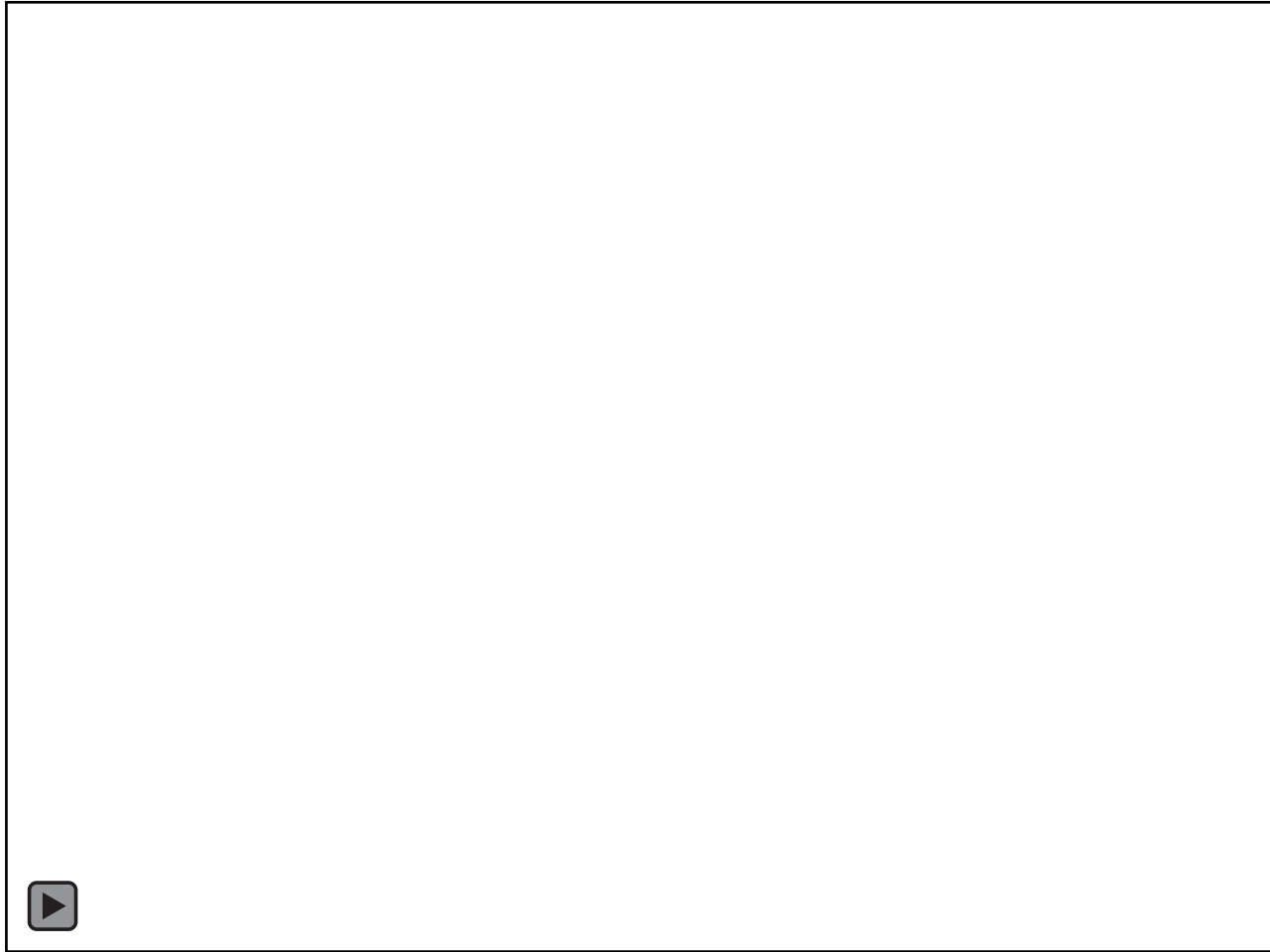


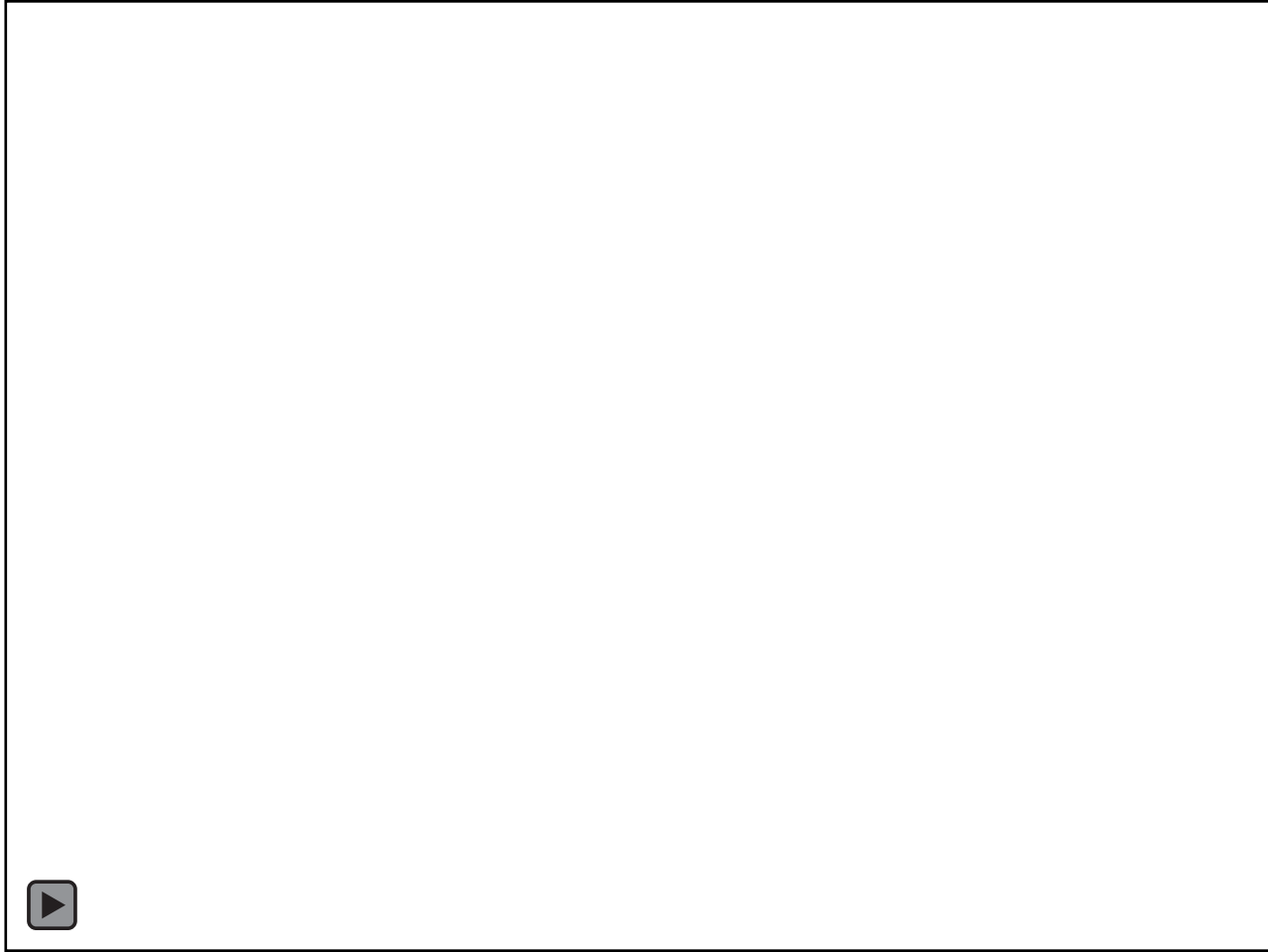


- Επιβεβαίωση στόχου



























Πρόγραμμα 14^{ης} Εκπαιδευτικής Εβδομάδος
Ελλήνων Ειδικευομένων Ουρολόγων
18-22 Φεβρουαρίου 2019
Ξενοδοχείο Athens Marriott

1^η Ημέρα - Δευτέρα 18 Φεβρουαρίου 2019

Καρκίνος του προστάτη και Συμπτώματα από το κατώτερο ουροποιητικό στους άνδρες

09:30 - 11:00 Θεραπεία εντοπισμένης νόσου

09.30-09.50 Ενεργή παρακολούθηση / **Ε. Φραγκιάδης**

09.50-10.10 Χειρουργική θεραπεία / **Μ. Καραβιτάκης**

10.10-10.30 Ακτινοβολία / **Ε. Μαραγκουδάκης**

10.30-10.50 Εστιασμένη θεραπεία / **Ι. Βαρκαράκης**

10:50-11:00 Ερωτήσεις - συζήτηση

ΕΥΧΑΡΙΣΤΩ