

Hospital Mãe de Deus

**Quais os resultados clínicos e efeitos colaterais
causados em radioterapia hipofracionada de
próstata**

Dra Andréa Barleze da Costa

**Radio-oncologista coordenadora Radioterapia Hospital Mãe de Deus – Porto
Alegre RS**



**HOSPITAL DO CÂNCER
MÃE DE DEUS**
SISTEMA DE SAÚDE MÃE DE DEUS

INDICAÇÕES DE TRATAMENTO

Definitions

Conventional Fractionation

Fraction size 180-200 cGy

Moderate Hypofractionation

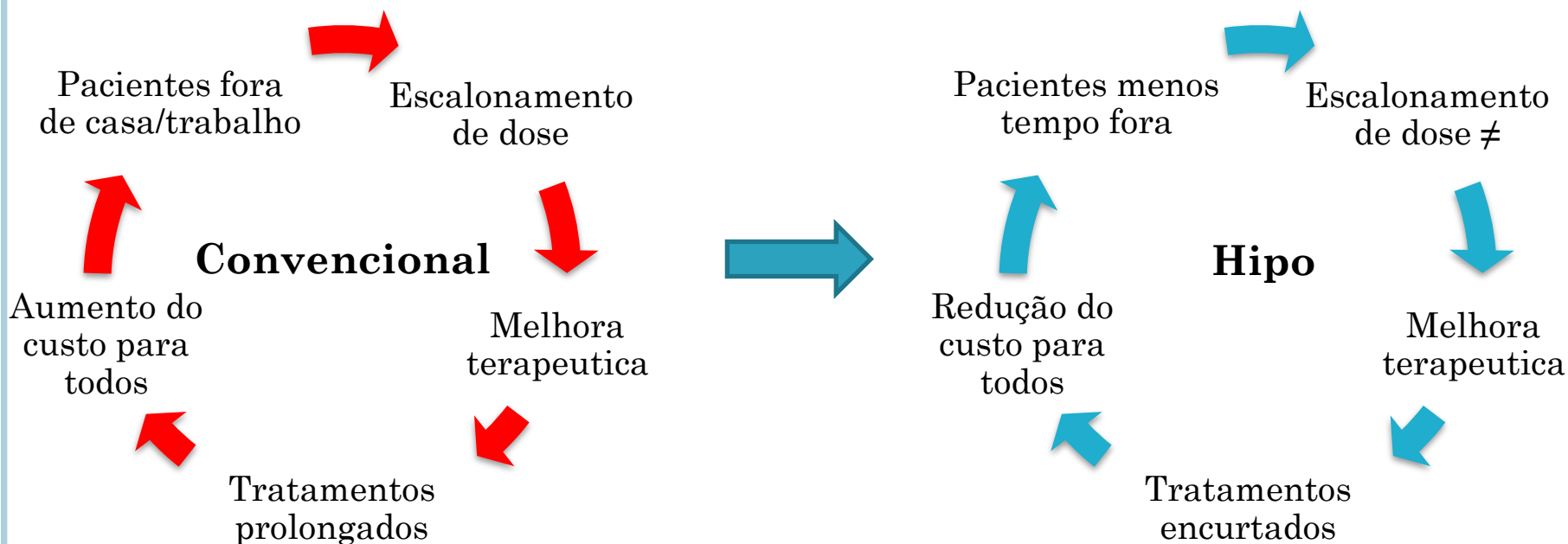
Fraction size 240-340 cGy

Ultrahypofractionation (SBRT, SABR)

Fraction size ≥ 500 cGy



RADIOTERAPIA - HIPOFRACIONAMENTO



INDICAÇÕES DE TRATAMENTO

Indicações

1. Hipofracionamento moderado
2. Hipofracionamento extremo

○ Considerar diversos fatores

Paciente (estágio, volume prostático, sintomas urinários, expectativas...)

Literatura

Aspectos técnicos

Segurança da equipe



INDICAÇÕES DE TRATAMENTO

- **Hipofracionamento moderado :**

Todo paciente com neoplasia de próstata não operada

Operados: estudos iniciais, faltam evidências fase III

- **Hipofracionamento extremo :**

Estabelecido para riscos baixo e intermediário

Evidência inicial no resgate / reirradiação

Doença oligometastática

Necessidade de equipe e tecnologia de ponta



PRINCIPAIS ESTUDOS EM HIPOFRACIONAMENTO



PRINCIPAIS ESTUDOS HIPOFRACIONAMENTO

Moderado, principais estudos

CHHiP

(Conventional or *H*yperfractionated *H*igh-dose *i*ntensity-modulated radiotherapy for *P*rostate cancer) (CRUK/06/016)



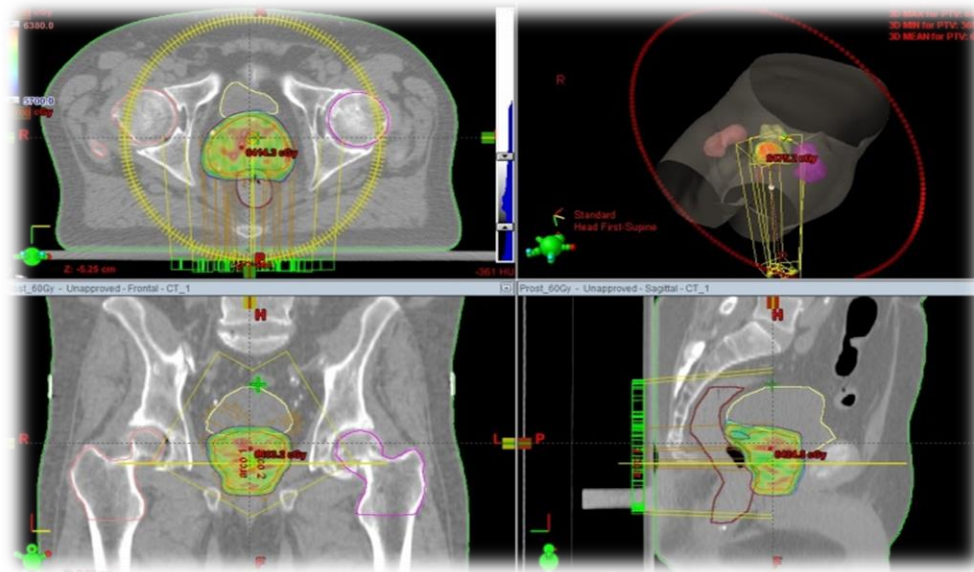
NRG ONCOLOGY

NRG Oncology RTOG 0415: A Randomized Phase III Non-Inferiority Study Comparing Two Fractionation Schedules in Men with Low-Risk Prostate Cancer



A randomized trial of a shorter radiation fractionation schedule for the treatment of localized prostate cancer

OCOG / TROG **PRO**state Fractionated Irradiation Trial



Fracionamento
convencional:

33 a 39 frações



Hipofracionamento:

20 frações



PRINCIPAIS ESTUDOS HIPOFRACIONAMENTO

Conventional versus hypofractionated high-dose intensity-modulated radiotherapy for prostate cancer: 5-year outcomes of the randomised, non-inferiority, phase 3 CHHiP trial



David Dearnaley, Isabel Syndikus, Helen Mossop, Vincent Khoo, Alison Birtle, David Bloomfield, John Graham, Peter Kirkbride, John Logue, Zafar Malik, Julian Money-Kyrle, Joe M O'Sullivan, Miguel Panades, Chris Parker, Helen Patterson*, Christopher Scrase, John Staffurth, Andrew Stockdale, Jean Tremlett, Margaret Bidmead, Helen Mayles, Olivia Naismith, Chris South, Annie Gao, Clare Cruickshank, Shama Hassan, Julia Pugh, Clare Griffin, Emma Hall, on behalf of the CHHiP Investigators

- Ensaio clínico randomizado, 71 centros, UK , Irlanda, Suíça e Nova Zelândia.
- Seguimento médio 62,4 meses
- **Desfecho primário: Tempo para falha bioquímica ou clínica**
- Não inferioridade
- **Riscos baixo a alto (cT1b – cT3a)** Inelegíveis T3 com Gleason 8, ou expectativa de vida < 10 anos





PRINCIPAIS ESTUDOS HIPOFRACIONAMENTO

	74 Gy in 37 fractions (N=1065)	60 Gy in 20 fractions (N=1074)	57 Gy in 19 fractions (N=1077)
(Continued from previous column)			
Median duration of radiotherapy (days)	53 (51-55)	29 (28-29)	28 (27-28)
Radiotherapy planning			
Forward planned	626 (59%)	624 (58%)	626 (58%)
Inverse planned	304 (29%)	337 (31%)	322 (30%)
Unavailable	135 (13%)	113 (11%)	129 (12%)
Radiotherapy delivery			
No image guidance	563 (53%)	568 (53%)	563 (52%)
Image-guided	312 (29%)	322 (30%)	326 (30%)
Unavailable	190 (18%)	184 (17%)	188 (17%)

Conventional versus hypofractionated high-dose intensity-modulated radiotherapy for prostate cancer: 5-year outcomes of the randomised, non-inferiority, phase 3 CHHiP trial

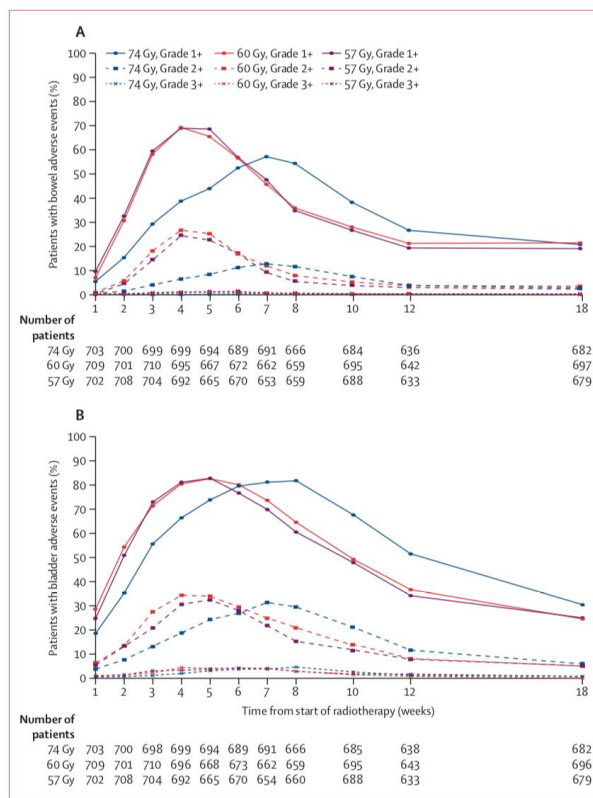
David Dearnaley, Isabel Syndikus, Helen Mossop, Vincent Khoo, Alison Birtle, David Bloomfield, John Graham, Peter Kirkbride, John Logue, Zafar Malik, Julian Money-Kyrle, Joe M O'Sullivan, Miguel Panades, Chris Parker, Helen Patterson*, Christopher Scrase, John Staffurth, Andrew Stockdale, Jean Tremlett, Margaret Bidmead, Helen Mayles, Olivia Naismith, Chris South, Annie Gao, Clare Cruickshank, Shama Hassan, Julia Pugh, Clare Griffin, Emma Hall, on behalf of the CHHiP Investigators

- ✓ Trial 1:1:1
- ✓ Protocolo bastante completo
- ✓ 5 anos de seguimento
- ✓ > 50% sem IGRT (portal image)
- ✓ ≈ 60% com técnica 3DCRT



Dearnaley et al. Lancet Oncol. 2016

PRINCIPAIS ESTUDOS HIPOFRACIONAMENTO



- **Maior toxicidade TGI no pico para hipofracionamento**

- **RTOG ≥ 2**

25% 74 Gy

38% 60 Gy ($p < 0,0001$)

38% 57 Gy ($p < 0,0001$)

GU $\geq 2 \rightarrow$ idêntica

46% 74 Gy

49% 60 Gy

46% 57Gy

Em 18 meses, toxicidades idênticas entre os grupos, $< 3\%$



PRINCIPAIS ESTUDOS HIPOFRACIONAMENTO

PROFIT TRIAL

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Randomized Trial of a Hypofractionated Radiation Regimen for the Treatment of Localized Prostate Cancer

Charles N. Catton, Himu Lukka, Chu-Shu Gu, Jarad M. Martin, Stéphane Supiot, Peter W.M. Chung, Glenn S. Bauman, Jean-Paul Bahary, Shahida Ahmed, Patrick Cheung, Keen Hun Tai, Jackson S. Wu, Matthew B. Parliament, Theodoros Tsakiridis, Tom B. Corbett, Colin Tang, Ian S. Dayes, Pdraig Warde, Tim K. Craig, Jim A. Julian, and Mark N. Levine

- Fase III, randomizado multicêntrico : Canadá, Austrália e França
- 6 anos seguimento. Não-inferioridade
- **Risco intermediário**
- **Desfecho primário: Falha bioquímica clínica**

Catton N. et al, 2016 J. Clin Oncol.



PRINCIPAIS ESTUDOS HIPOFRACIONAMENTO

Table 3. Genitourinary Toxicity by Period, Treatment, and Grade

Grade	Acute* Toxicity (No. [%])		Late† Toxicity (No. [%])	
	Short (n = 608)	Standard (n = 598)	Short (n = 608)	Standard (n = 598)
None	150 (25)	143 (24)	310 (51)	299 (50)
1	273 (45)	272 (46)	162 (27)	165 (28)
2	161 (27)	159 (27)	122 (20)	116 (19)
3	24 (3.9)	24 (4.0)	12 (2.0)	17 (2.8)
4	0	0	1 (0.2)	1 (0.2)

*Acute period = worst grade during the first 14 weeks.

†Late period = worst grade from 6 months onward.

Table 4. GI Toxicity by Period, Treatment, and Grade

Grade	Acute* Toxicity (No. [%])		Late† Toxicity (No. [%])	
	Short (n = 608)	Standard (n = 598)	Short (n = 608)	Standard (n = 598)
None	249 (41)	286 (48)	355 (58)	311 (52)
1	260 (43)	250 (42)	199 (33)	204 (34)
2	95 (16)	59 (10)	45 (7.4)	66 (11)
3	4 (0.7)	3 (0.5)	9 (1.5)	16 (2.7)
4	0	0	0	1 (0.2)

*Acute period = worst grade during the first 14 weeks.

†Late period = worst grade from 6 months onward.

Considerada Idêntica

GU agudo ≥ 3 : 4%

ambos

GU tardio : 3% e 2,1% (60/20)

TGI

G2 agudo $\rightarrow$ Hipo ($p : 0,003$)

G2 tardio $\rightarrow$ Padrão ($p : 0,006$)



INDICAÇÕES DE TRATAMENTO - MODERADO

Hypofractionated RT for Localized Prostate Cancer: An ASTRO, ASCO, and AUA Evidence-Based Guideline

Introduction and Process

Scott Morgan, MD, MSc, FRCPC

Division of Radiation Oncology

The Ottawa Hospital and University of Ottawa

Ottawa, Ontario, Canada

  #ASTRO18

2018 ANNUAL MEETING | HENRY B. GONZALEZ CONVENTION CENTER | SAN ANTONIO



INDICAÇÕES DE TRATAMENTO - MODERADO

KQs 1 and 2: Indications and dose-fractionation for moderately hypofractionated RT

Karen Hoffman, MD, MHSC, MPH
Department of Radiation Oncology
University of Texas MD Anderson Cancer Center
Houston, Texas



2018 ANNUAL MEETING | HENRY B. GONZALEZ CONVENTION CENTER | SAN ANTONIO



INDICAÇÕES DE TRATAMENTO - MODERADO

Moderate hypofxn provides similar cancer control



Trial	N	Design	Study arms/ EQ2	Cancer Risk Group	ADT Use	Median Fup	Cancer Control
NON-INFERIORITY TRIALS							
CHHiP	3216	Multicenter Non-inferiority. 1° endpoint: biochemical or clinical failure-free rate	7400 in 200 cGy/ 7400 cGy 6000 in 300 cGy/ 7700 cGy 5700 in 300 cGy/ 7300 cGy	15% Low 73% Int 12% High	97% 3-6 mo	5.2 yrs	6000 in 300 cGy Non-inferior to 7400 in 200 cGy
PROFIT	608	Multicenter Non-inferiority. 1° endpoint: biochemical- clinical failure	7800 in 200 cGy/ 7800 cGy 6000 in 300 cGy/ 7700 cGy	All Int	None	6 yrs	Moderate Hypofractionation Non-inferior

#ASTRO18

2018 ANNUAL MEETING | HENRY B. GONZALEZ CONVENTION CENTER | SAN ANTONIO



INDICAÇÕES DE TRATAMENTO - MODERADO

Moderate hypofxn provides similar cancer control

Trial	N	Design	Study arms/ EQ2	Cancer Risk Group	ADT Use	Median Fup	Cancer Control
RTOG 0415	1115	Multicenter Non- inferiority. 1º endpoint: disease- free survival	7380 in 180 cGy/ 7000 cGy 7000 in 250 cGy/ 8000 cGy	All Low	None	5.8 yrs	Moderate Hypofractionation Non-inferior
SUPERIORITY TRIALS							
HYPRO	820	Multicenter Superiority. 1º endpoint: relapse free survival	7800 in 200 cGy/ 7800 cGy 6460 in 340 cGy (3/wk) / 8700 cGy	26% Int 74% High	67% Var- iable	5 yrs	No Significant Difference



[#ASTRO18](#)

2018 ANNUAL MEETING | HENRY B. GONZALEZ CONVENTION CENTER | SAN ANTONIO



INDICAÇÕES DE TRATAMENTO - MODERADO

KQ1 Recommendation Statements

Prostate cancer control outcomes: Impact of risk stratification group

- **KQ1A:** In men with **low-risk** prostate cancer who decline active surveillance and receive EBRT to the prostate with or without radiation to the seminal vesicles, moderate hypofractionation should be offered.
- **KQ1B:** In men with **intermediate-risk** prostate cancer receiving EBRT to the prostate with or without radiation to the seminal vesicles, moderate hypofractionation should be offered.

Recommendation strength	Quality of evidence	Consensus
Strong	High	100%

Recommendation strength	Quality of evidence	Consensus
Strong	High	100%

  #ASTRO18

2018 ANNUAL MEETING | HENRY B. GONZALEZ CONVENTION CENTER | SAN ANTONIO



INDICAÇÕES DE TRATAMENTO - MODERADO

KQ1 Recommendation Statements

Prostate cancer control outcomes: Impact of risk stratification group

- **KQ1C:** In men with high-risk prostate cancer receiving EBRT to the prostate, but not including pelvic lymph nodes, moderate hypofractionation should be offered.

Recommendation strength	Quality of evidence	Consensus
Strong	High	94%

Recommendations for or against the use of elective pelvic nodal EBRT in patients with high-risk cancer are beyond the scope of this guideline.

INDICAÇÕES DE TRATAMENTO - MODERADO

KQ1 Recommendation Statements

Toxicity and quality of life

- **KQ1E:** Men should be counseled about the small increased risk of acute GI toxicity with moderate hypofractionation. Moderately hypofractionated EBRT has a similar risk of acute and late GU and late GI toxicity compared to conventionally fractionated EBRT. However, physicians should discuss the limited follow-up beyond five years for most existing RCTs evaluating moderate hypofractionation.

Recommendation strength	Quality of evidence	Consensus
Strong	High	100%

  #ASTRO18

2018 ANNUAL MEETING | HENRY B. GONZALEZ CONVENTION CENTER | SAN ANTONIO

Aumento discreto toxicidade GI aguda, tardios GU e GI idênticas



INDICAÇÕES DE TRATAMENTO - MODERADO

KQs 3 and 4: Indications and dose-fractionation for ultrahypofractionated RT

D. Andrew Loblaw, MD, MSc, FRCPC

Department of Radiation Oncology
Institute of Health Policy, Management and Evaluation

University of Toronto

Toronto, Ontario, Canada

  #ASTRO18

2018 ANNUAL MEETING | HENRY B. GONZALEZ CONVENTION CENTER | SAN ANTONIO



INDICAÇÕES DE TRATAMENTO

- **Ultrahipofracionamento**

Baixo risco recomendação em 88%

Risco intermediário recomendação 94 %

- IMRT : Recomendada por 100%

- IGRT : Recomendada por 100%

Resumo : IMRT e IGRT obrigatórias



ULTRAHIPOFRACIONAMENTO

Statement KQ3A

In men with low-risk prostate cancer who decline active surveillance and choose active treatment with EBRT, ultrahypofractionation may be offered as an alternative to conventional fractionation.

- Strength of recommendation: Conditional
- Quality of evidence: Moderate
- Consensus: 88%

Baixo risco = Oferecer SBRT

Intermediário = Discutir SBRT

ULTRAHIPOFRACIONAMENTO

Estudos fase III em 2019 evidenciam segurança e comparável controle bioquímico

- ✓ HYPO-RT trial
- ✓ PACE B trial



ULTRAHIPOFRACIONAMENTO

Ultra-hypofractionated versus conventionally fractionated radiotherapy for prostate cancer: 5-year outcomes of the HYPO-RT-PC randomised, non-inferiority, phase 3 trial



Anders Widmark, Adalsteinn Gunnlaugsson, Lars Beckman, Camilla Thellenberg-Karlsson, Morten Hoyer, Magnus Lagerlund, Jon Kindblom, Claes Ginman, Bengt Johansson, Kirsten Björnling, Mihajl Seke, Måns Agrup, Per Fransson, Björn Tavelin, David Norman, Björn Zackrisson, Harald Anderson, Elisabeth Kjellén, Lars Franzén, Per Nilsson

1200 pacientes com idade até 75a

Intermediário/alto risco

Conventional: 2.0 Gy x 39 = 78.0 Gy

versus

HYPO: 6.1 Gy x 7 = 42.7 Gy

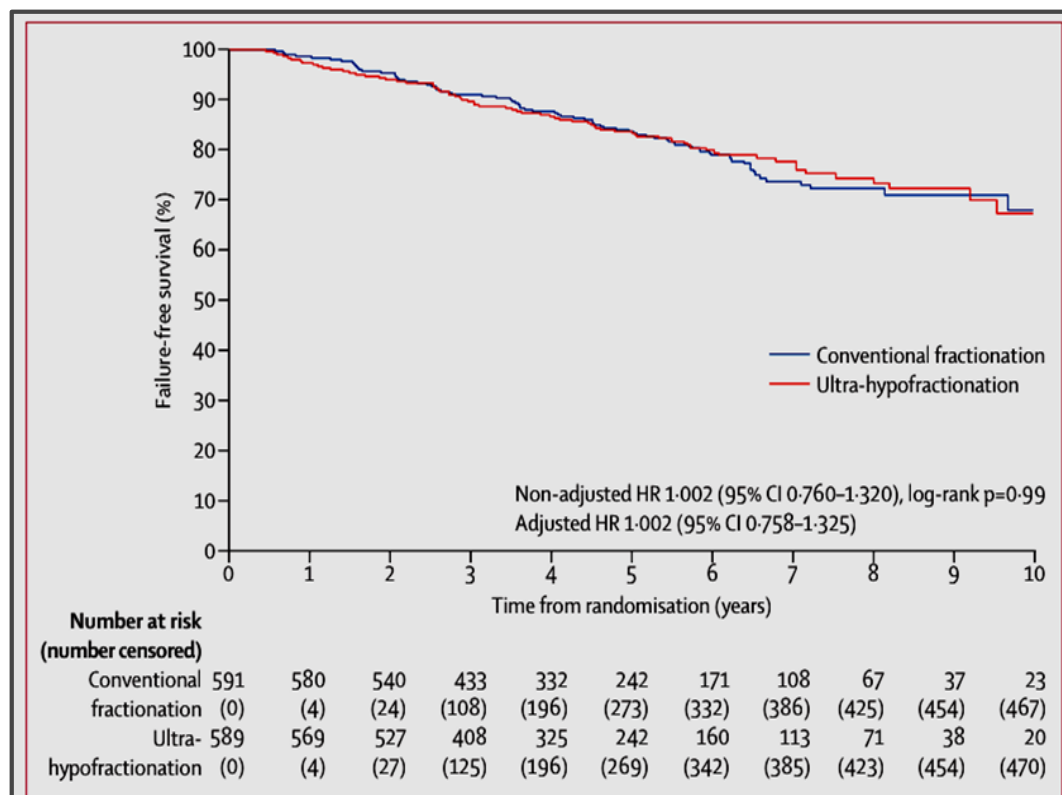


ULTRAHIPOFRACIONAMENTO

RESULTADOS

Follow-up mediano = 5a

SG 95% RTconv
vs 96% UltraRT



ULTRAHIPOFRACIONAMENTO

- ✓ **Toxicidade urinária** grau 2 ou + ao término da radioterapia no braço ULTRA **28%** vs **23%** ($p=0.057$)
- ✓ **Toxicidade urinária** grau 2 ou + ao final do 1 ano no braço ULTRA **6%** vs **2%** ($p=0.0037$)
- ✓ Sem diferença na toxicidade urinária em 5 anos (5% ambos braços)
- ✓ Sem diferença na toxicidade retal
- ✓ Sem diferença em disfunção sexual

Interpretation Ultra-hypofractionated radiotherapy is non-inferior to conventionally fractionated radiotherapy for intermediate-to-high risk prostate cancer regarding failure-free survival. Early side-effects are more pronounced with ultra-hypofractionation compared with conventional fractionation whereas late toxicity is similar in both treatment groups. The results support the use of ultra-hypofractionation for radiotherapy of prostate cancer.

ULTRAHIPOFRACIONAMIENTO

Intensity-modulated fractionated radiotherapy versus stereotactic body radiotherapy for prostate cancer (PACE-B): acute toxicity findings from an international, randomised, open-label, phase 3, non-inferiority trial



Douglas H Brand, Alison C Tree*, Peter Ostler, Hans van der Voet, Andrew Loblaw, William Chu, Daniel Ford, Shaun Tolan, Suneil Jain, Alexander Martin, John Staffurth, Philip Camilleri, Kiran Kancherla, John Frew, Andrew Chan, Ian S Dayes, Daniel Henderson, Stephanie Brown, Clare Cruickshank, Stephanie Burnett, Aileen Duffton, Clare Griffin, Victoria Hinder, Kirsty Morrison, Olivia Naismith, Emma Hall, Nicholas van As, on behalf of the PACE Trial Investigators*



ULTRAHIPOFRACIONAMENTO

Intensity-modulated fractionated radiotherapy versus stereotactic body radiotherapy for prostate cancer (PACE-B): acute toxicity findings from an international, randomised, open-label, phase 3, non-inferiority trial



Douglas H Brand*, Alison C Tree*, Peter Ostler, Hans van der Voet, Andrew Loblaw, William Chu, Daniel Ford, Shaun Tolan, Suneil Jain, Alexander Martin, John Staffurth, Philip Camilleri, Kiran Kancharla, John Frew, Andrew Chan, Ian S Dayes, Daniel Henderson, Stephanie Brown, Clare Cruickshank, Stephanie Burnett, Aileen Duffton, Clare Griffin, Victoria Hinder, Kirsty Morrison, Olivia Naismith, Emma Hall, Nicholas van As, on behalf of the PACE Trial Investigators

874 pacientes

**Risco
baixo/intermediário**
(Gleason 4+3 excluídos)

R
A
N
D
O
M
I
Z
A
D
O
S

Conventional: 78.0 Gy/ 39fr or
Hypo: 62Gy / 20ft (n = 441/432)

SBRT: 7,25 Gy x 5 = 36,25 Gy
(LINAC ou Cyberknife) (n = 433/415)

ULTRAHIPOFRACIONAMENTO

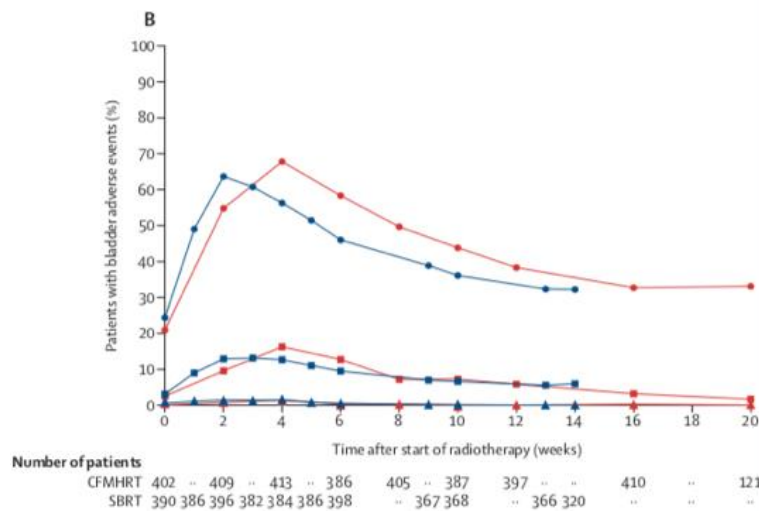
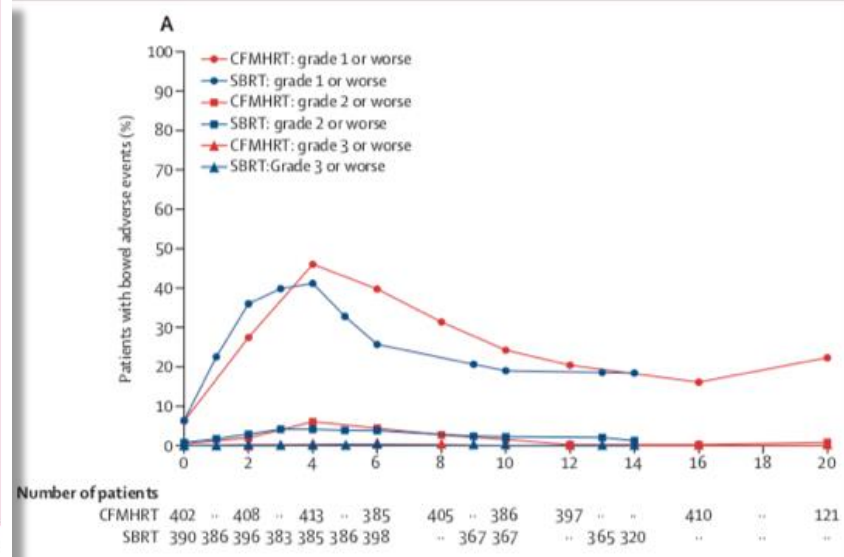


Figure 2: Acute Radiation Therapy Oncology Group toxicity for gastrointestinal (A) and genitourinary (B) systems



	Conventionally fractionated or moderately hypofractionated radiotherapy (n=432)				Stereotactic body radiotherapy (n=415)			
	Grade 1	Grade 2	Grade 3	Grade 4	Grade 1	Grade 2	Grade 3	Grade 4
Gastrointestinal	264 (61%)	49 (11%)	4 (1%)	0	219 (53%)	42 (10%)	1 (<1%)	0
Genitourinary	254 (59%)	111 (26%)	6 (1%)	1 (<1%)	236 (57%)	86 (21%)	8 (2%)	2 (<1%)

Data are n (%). No death due to adverse events were reported.

Table 2: Radiation Therapy Oncology Group adverse events

ULTRAHIPOFRACIONAMENTO

KQ7 Recommendation Statement: IGRT

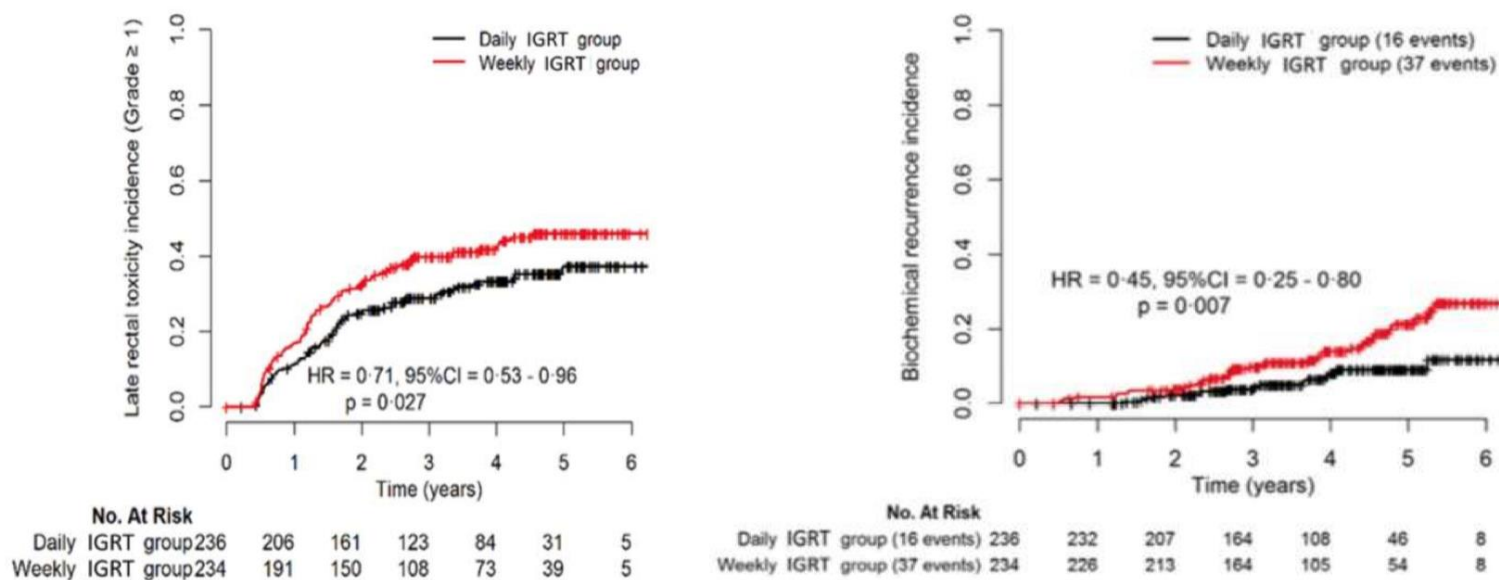
- **KQ7A:** IGRT is universally recommended when delivering moderately or ultrahypofractionated EBRT.

Recommendation strength	Quality of evidence	Consensus
Strong	Moderate	100%

EXIGÊNCIA DE IGRT

ULTRAHIPOFRACIONAMENTO

Daily vs. Weekly IGRT: Phase III Trial



de Crevoisier et al., IJROBP In Press

2018 ANNUAL MEETING | HENRY B. GONZALEZ CONVENTION CENTER | SAN ANTONIO

#ASTRO18

ULTRAHIPOFRACIONAMENTO

KQ8 Recommendation Statement: Technique

- **KQ8A:** Non-modulated 3-D CRT techniques are not recommended when delivering moderately or ultrahypofractionated prostate EBRT.

Recommendation strength	Quality of evidence	Consensus
Strong	Moderate	100%

TÉCNICAS MODULADAS

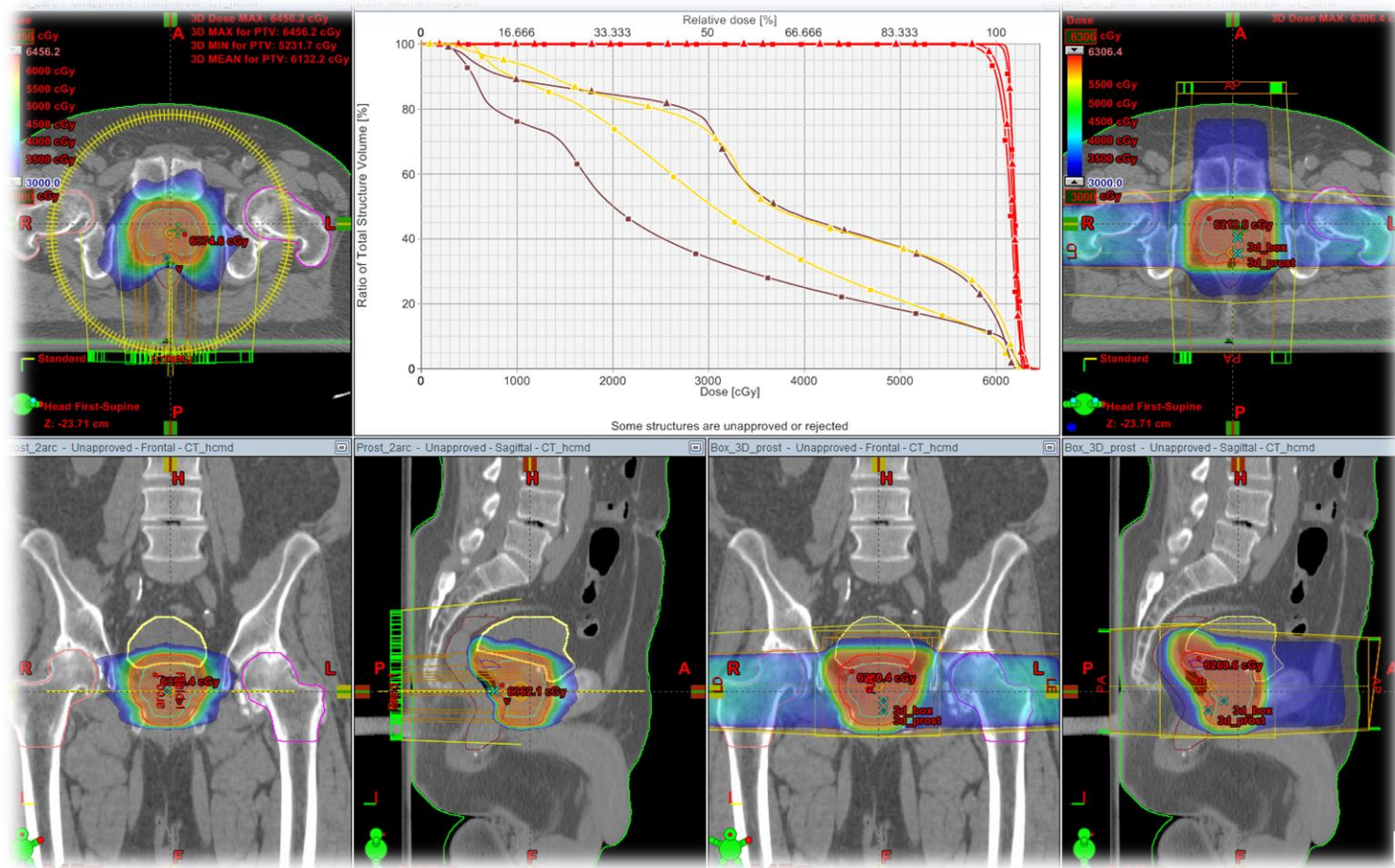
QUESTÕES TÉCNICAS NO HIPOFRACIONAMENTO

- ✓ Técnica 3D, IMRT, VMAT
- ✓ Literatura
- ✓ Estar ciente do **SEU** sistema de tratamento
- ✓ Equipe multidisciplinar
- ✓ **IGRT**
- ✓ Estudos clínicos encorajados



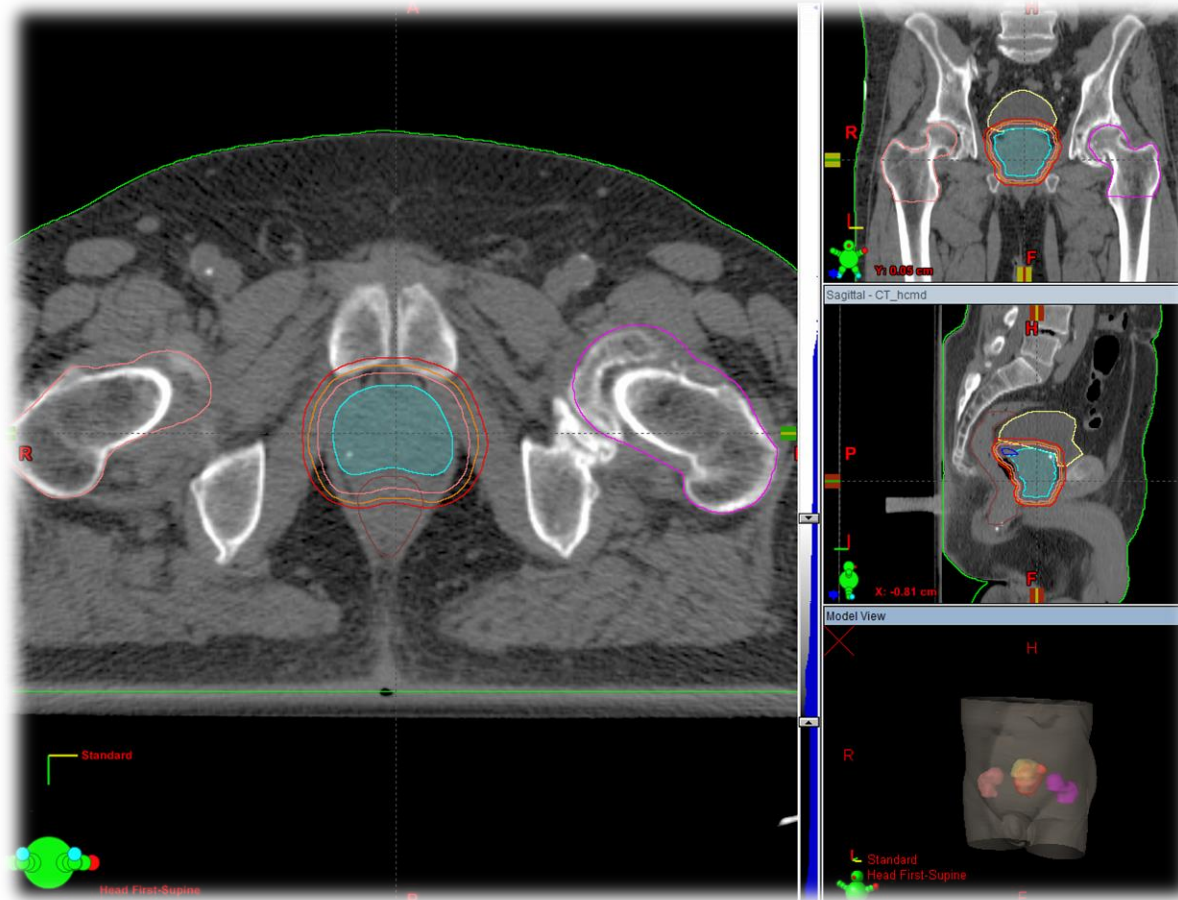
QUESTÕES TÉCNICAS NO HIPOFRACIONAMENTO

Técnicas de tratamento – 3DCRT vs. Rapidarc



QUESTÕES TÉCNICAS NO HIPOFRACIONAMENTO

Definição de PTV – tamanho da importância



$$PTV_{5mm} = 182cm^3$$

+27%

$$PTV_{7mm} = 231cm^3$$

+26%

$$PTV_{1cm/8mm} = 291cm^3$$

+60%

SETUP E MARGENS - PRÓSTATA



QUESTÕES TÉCNICAS NO HIPOFRACIONAMENTO

Estudo HMD

- 95 CBCTs desenhados após ajuste por parâmetros ósseos

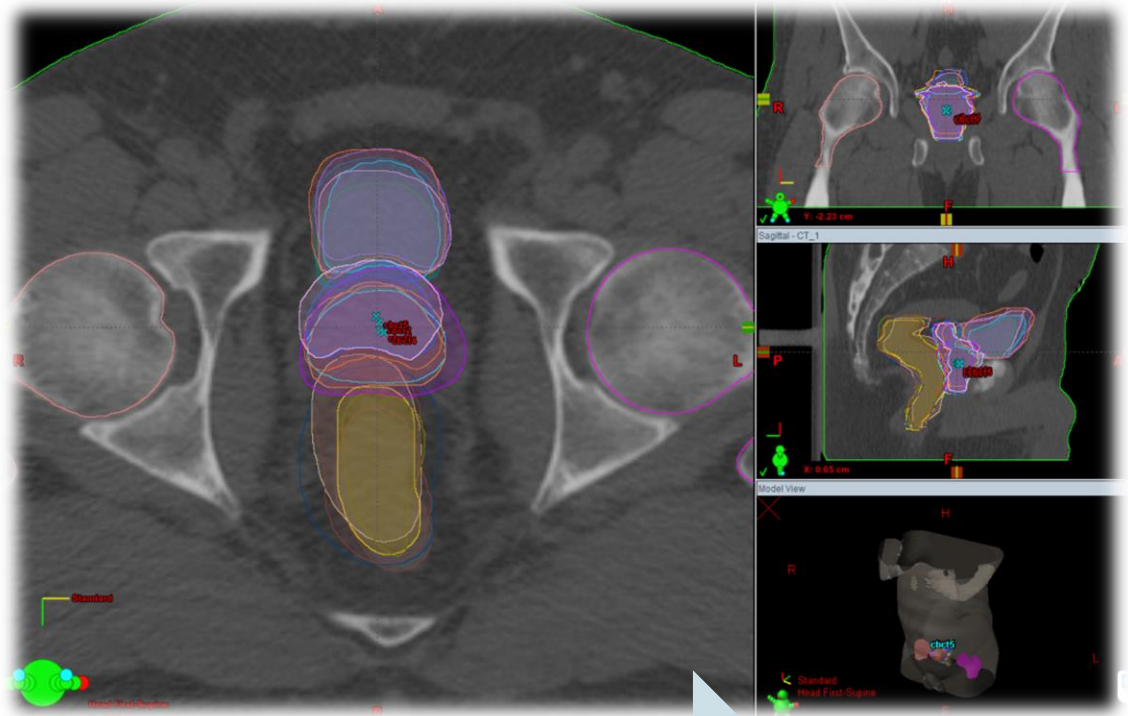


Imagem Planar e Ajuste

CBCT sem ajuste (para registro)

Tratamento

Desenho das estruturas no CBCT

Análise da variação interna dos órgãos

SETUP E MARGENS - PRÓSTATA

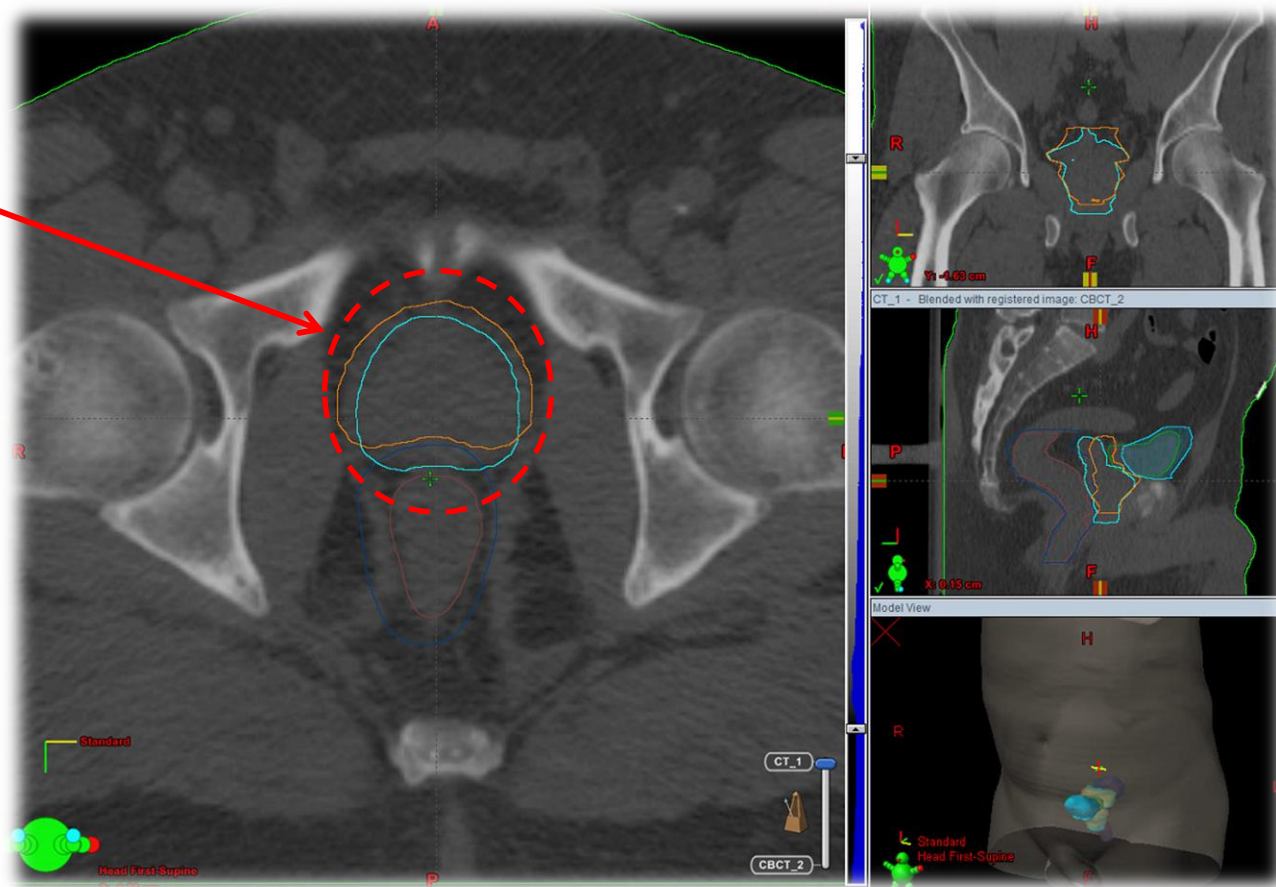


QUESTÕES TÉCNICAS NO HIPOFRACIONAMENTO

Variação da próstata e OARs – Mesmo após ajuste ósseo

Necessidade
de PTV:

- ✓ Tipo de preparo (dieta)
- ✓ Modalidade de Imagem
- ✓ Protocolo de imagens

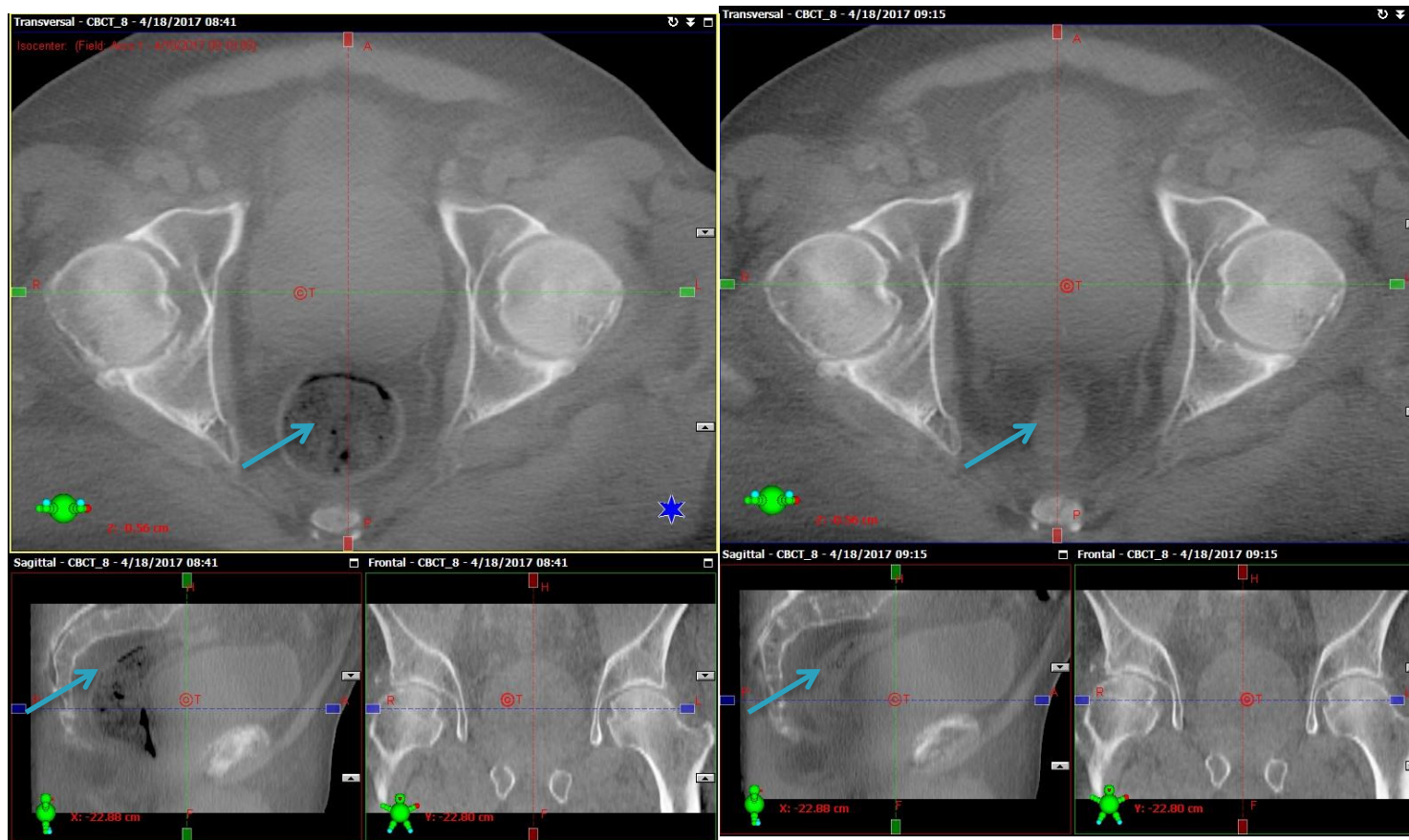


SETUP E MARGENS - PRÓSTATA



QUESTÕES TÉCNICAS NO HIPOFRACIONAMENTO

Exemplos de controle por imagem de tomografia CBCT



8:40

9:15

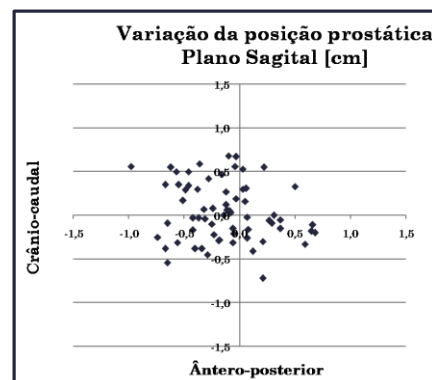
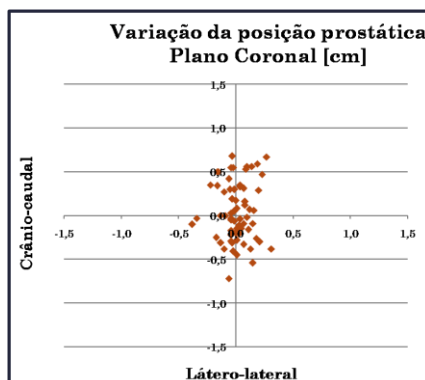
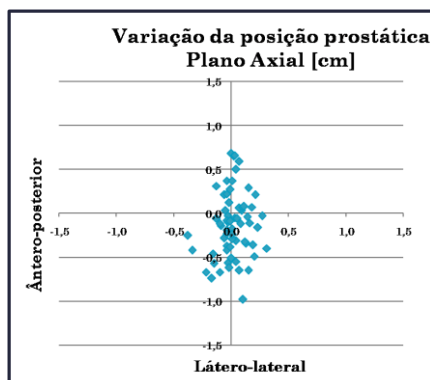


QUESTÕES TÉCNICAS NO HIPOFRACIONAMENTO



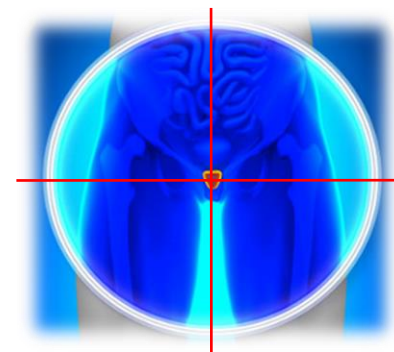
Estudo HMD - resultado

Deslocamento médio da próstata (após ajuste ósseo):
1mm, 3mm e 3mm (LAT, CC, AP)



Deslocamento da próstata (2σ):
3mm, 7mm e 7mm (LAT, CC, AP)

Comparável com literatura¹



1. Mayyas, Essa, et al. "Evaluation of multiple image-based modalities for image-guided radiation therapy (IGRT) of prostate carcinoma: A prospective study." *Medical physics* 40.4 (2013).

QUESTÕES TÉCNICAS NO HIPOFRACIONAMENTO

Critérios e seleção para reduzir toxicidade

Toxicity of SBRT: Critical Factors and Selection Criteria For Reducing Complications

Sean P. Collins, M.D., Ph.D.
Associate Professor
Georgetown University Hospital

Análise crítica das evidências atuais

2018 ANNUAL MEETING | HENRY B. GONZALEZ CONVENTION CENTER | SAN ANTONIO

  #ASTRO18



QUESTÕES TÉCNICAS NO HIPOFRACIONAMENTO

Critérios e seleção para reduzir toxicidade

Predictors of Acute Urinary Symptom Flare

- Definition

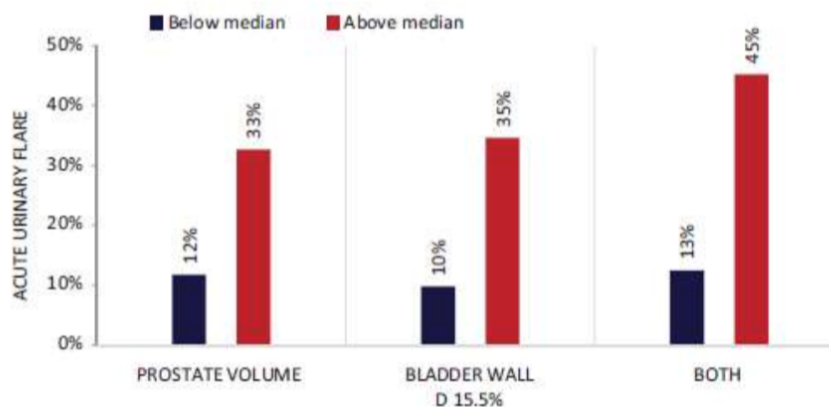
- IPSS > 15

- > 5 points above baseline

- Predictors

- Prostate Volume > 36 cc

- Bladder wall D15.5%



■ Repka M., *Acta. Oncol.*, 2017



QUESTÕES TÉCNICAS NO HIPOFRACIONAMENTO

Critérios e seleção para reduzir toxicidade

Predictors of Symptomatic Rectal Bleeding Following SBRT

- Dose and Treatment Volume

- 35 Gy/prostate 4.9%
- 40 Gy/prostate 27.2%
- 40 Gy/prostate and SV 42.1%

- Volume of Rectum Receiving 38 Gy

- < 2 cc 8.7%
- $\geq$ 2 cc 28.4%

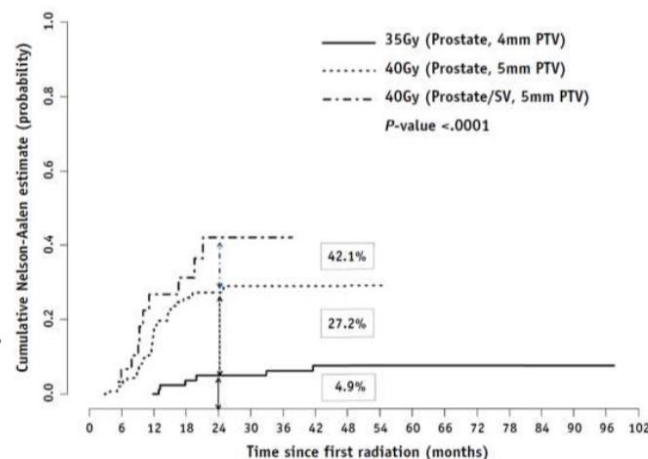


Fig. 1. Two-year cumulative high-grade hematochezia for patients with different clinical targets and planning target volume margins (PTV).

■ Musunura, IJROBP, 2016

Twitter Facebook #ASTRO18

2018 ANNUAL MEETING | HENRY B. GONZALEZ CONVENTION CENTER | SAN ANTONIO



HIPOFRACIONAMENTO DE PRÓSTATA

Cenários :

- ✓ Hipofracionamento moderado próstata presente
- ✓ Hipofracionamento moderado leito prostático
- ✓ Ultra-hipofracionamento – *SBRT*
- ✓ Ultra-hipofracionamento em reirradiação



HIPOFRACIONAMENTO DE PRÓSTATA

Protocolo HMD

- ✓ Dieta específica com acompanhamento
- ✓ Tomografia (CBCT) diária
- ✓ Técnica de RapidArc®
- ✓ **60Gy / 20 frações para tratamento radical**
- ✓ **56Gy / 20 frações para tratamento de resgate**
- ✓ **45Gy / 20 frações para tratamento de drenagens, de forma concomitante**
- ✓ Rotina desde out/2016 (1º caso em out/15)



HIPOFRACIONAMENTO DE PRÓSTATA



HOSPITAL DO CÂNCER
MÃE DE DEUS
SISTEMA DE SAÚDE MÃE DE DEUS

PROTOCOLO INSTITUCIONAL



ETIQUETA DE IDENTIFICAÇÃO

PROTOCOLO DE TRATAMENTO DE RADIOTERAPIA HIPOFRACIONADA EM PACIENTES COM
CÂNCER DE PRÓSTATA

Hipofracionamento Moderado = 20x280cGy, com IGRT.

Médico Radio-oncologista: _____

Gleason: _____ Hormônioterapia: _____

PSA: _____ ECOG: _____

Incontinência urinária: _____ Função Eritr: _____

Hábito Intestinal: _____

Muito baixo risco ()	Baixo risco ()	Intermediário ()
T1 C Gleason ≤ 6 PSA < 10ng/mL Menos de 3 fragmentos positivos na biópsia, e menos de 50% de cada um dos fragmentos comprometidos.	T1 – T2a Gleason ≤ 6 PSA < 10ng/mL	T2b – T2c ou Gleason = 7 ou PSA = 10 a 20ng/mL

Alto Risco ()	Muito alto risco ()
T3a ou Gleason = 8 a 10 ou PSA > 20ng/mL	T3b – T4 ou Gleason padrão = 5 ou Mais do que 4 fragmentos da biópsia com Gleason de 8 a 10

Experiência clínica HCMD



ETIQUETA DE IDENTIFICAÇÃO

PROTOCOLO DE TRATAMENTO DE RADIOTERAPIA HIPOFRACIONADA EM PACIENTES COM
CÂNCER DE PRÓSTATA

Hipofracionamento Moderado = 20x300cGy, com IGRT.

TOXICIDADE					
	Grau 0	Grau 1	Grau 2	Grau 3	Grau 4
Bexiga	Nenhum	Atrofia epitelial leve Telangiectasia menor (hematúria microscópica)	Frequência moderada Telangiectasia generalizada Hematuria macrosscópica intermitente	Frequência grave e disúria Telangiectasia generalizada (frequentemente com petequias) Hematuria frequente Redução da capacidade da bexiga (<150 cc)	Necrose Bexiga contraída (capacidade <100 cc) Cistite hemorrágica grave
	Grau 0	Grau 1	Grau 2	Grau 3	Grau 4
Reto	Nenhum	Diarréia leve Cólicas leves Gruelamento intestinal 5 vezes por dia Leve descarga retal ou sangramento	Diarréia moderada e cólicas Movimento intestinal mais do que 5 vezes por dia Muco retal excessivo ou sangramento intermitente	Obstrução Sangramento *Requer cirurgia	Necrose Perfuração Fístula

Avaliação da toxicidade e PSA

Alta 270 dias
Data: __/__/__ Bexiga: __ Reto: __ PSA: __
30 dias 1 ano
Data: __/__/__ Bexiga: __ Reto: __ PSA: __
90 dias 450 dias
Data: __/__/__ Bexiga: __ Reto: __ PSA: __
180 dias 540 dias
Data: __/__/__ Bexiga: __ Reto: __ PSA: __



XX Congresso da Sociedade Brasileira de Radioterapia



HIPOFRACIONAMENTO DE PRÓSTATA

Casuística HMD – Hipofracionamento moderado definitivo e operados

- Número de pacientes de próstata hipofracionados HMD: **299**

Número de aplicações se
tratamentos convencionais:

10764

Número de aplicações em
tratamentos hipofracionados:

5980

$$10764 - 5980 = 4784$$



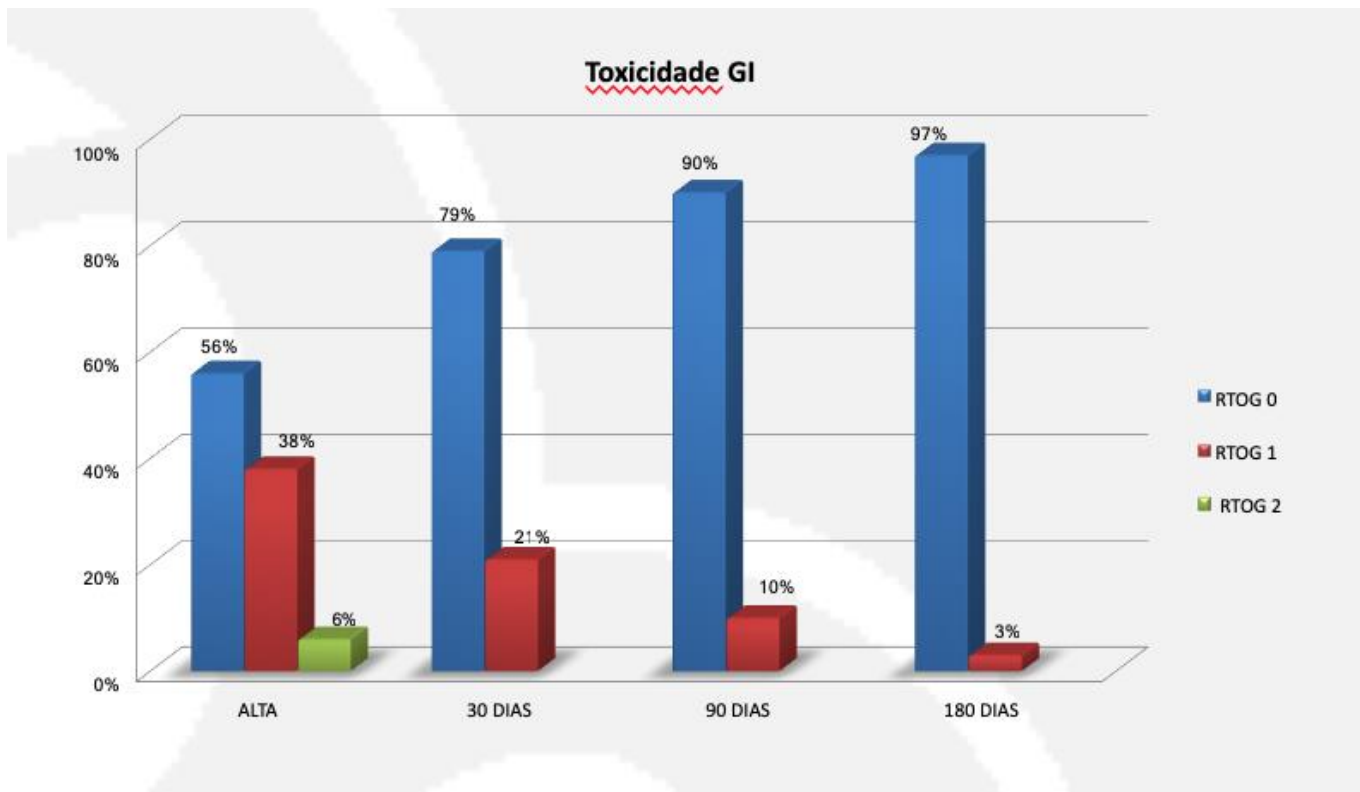
- 44% “visitas”
ao serviço

4784 aplicações = + 239 pacientes hipofracionados no
mesmo *slot* de agenda



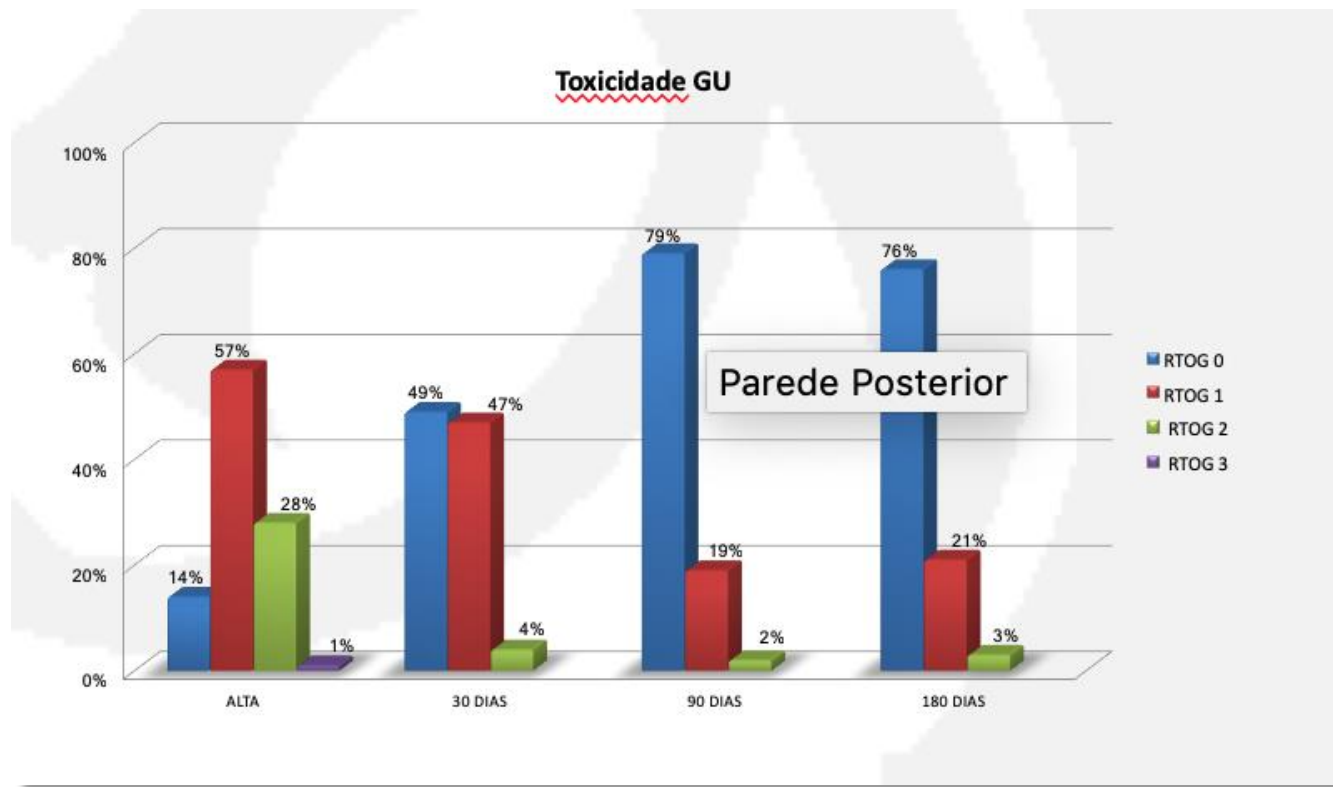
HIPOFRACIONAMENTO MODERADO

Pacientes não operados



HIPOFRACIONAMENTO MODERADO

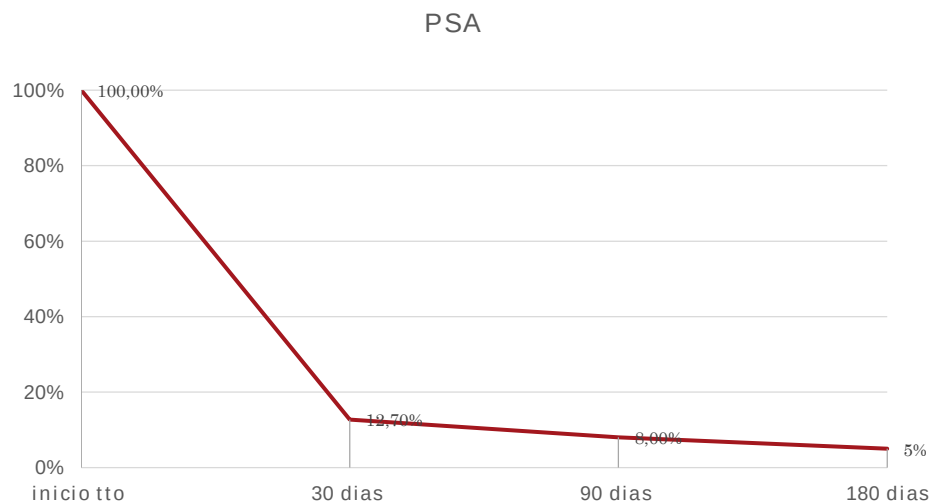
Pacientes não operados



HIPOFRACIONAMENTO MODERADO

Pacientes não operados

RESULTADOS - INDICADORES



HIPOFRACIONAMENTO MODERADO

Operado – Fossa prostática

Clinical Investigation

Hypofractionated IMRT of the Prostate Bed After Radical Prostatectomy: Acute Toxicity in the PRIAMOS-1 Trial

Sonja Katayama, MD,^{*} Thorbjørn Striecker,^{*} Kerstin Kessel,^{*} Florian Sterzing, MD,^{*,†} Gregor Habl, MD,^{*} Lutz Edler, MD,[‡] Juergen Debus, MD, PhD,^{*,†} and Klaus Herfarth, MD^{*}

^{*}Department of Radiation Oncology, University Hospital Heidelberg, Im Neuenheimer Feld, Heidelberg, Germany; [†]Department of Radiation Oncology, German Cancer Research Center, Im Neuenheimer Feld, Heidelberg, Germany; and [‡]Department of Biostatistics, German Cancer Research Center, Im Neuenheimer Feld, Heidelberg, Germany

Received Apr 14, 2014, and in revised form Jun 13, 2014. Accepted for publication Jul 11, 2014.



HIPOFRACIONAMENTO MODERADO

Operado – Fossa prostática

- ✓ **Atual :120 pacientes**, mínimo 1 ano seguimento
- ✓ Toxicidade RTOG G3 < 2%

Protocolo HMD

Dose definida : BED adaptado ao *PRIAMOS trial*

- ✓ 56Gy / 20 frações para tratamento de resgate
- ✓ 45Gy / 20 frações para tratamento de drenagens, de forma



HIPOFRACIONAMENTO MODERADO

Operado – Fossa prostática

Cancer Treatment Reviews 62 (2018) 91–96



ELSEVIER

Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

Cancer Treatment Reviews

journal homepage: www.elsevierhealth.com/journals/ctrv



Tumour Review

Hypofractionated radiotherapy for prostate cancer in the postoperative setting: What is the evidence so far?



Cristina Picardi^a, Ioan Perret^b, Raymond Miralbell^{a,b}, Thomas Zilli^{a,b,*}

^aDepartment of Radiation Oncology, Geneva University Hospital, Geneva, Switzerland

^bFaculty of Medicine, Geneva University, Switzerland



HIPOFRACIONAMENTO MODERADO

Operado – Fossa prostática

ANTICANCER RESEARCH 38: 1221-1230 (2018)
doi:10.21873/anticancer.12343

Review

Postoperative Hypofractionated Radiation Therapy in Prostate Carcinoma: A Systematic Review

GIAMBATTISTA SIEPE¹, MILLY BUWENGE¹, NAM P. NGUYEN², GABRIELLA MACCHIA³,
FRANCESCO DEODATO³, SAVINO CILLA⁴, GIAN C. MATTIUCCI⁵, ILARIA CAPOCACCIA¹,
SILVIA CAMMELLI¹, ALESSANDRA GUIDO¹, ALESSANDRA ARCELLI¹,
MARIA NTRETA¹, SARA GUERRI^{6*} and ALESSIO G. MORGANTI^{1*}

¹*Radiation Oncology Center, Department of Experimental, Diagnostic and Specialty Medicine –
DIMES, S. Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy;*

²*Department of Radiation Oncology, Howard University College of Medicine, Washington, DC, U.S.A.;*

³*Radiotherapy Unit, Fondazione "Giovanni Paolo II", Catholic University of Sacred Heart, Campobasso, Italy;*

⁴*Medical Physic Unit, Fondazione "Giovanni Paolo II", Catholic University of Sacred Heart, Campobasso, Italy;*

⁵*Radiation Oncology Department, Università Cattolica del Sacro Cuore, Rome, Italy;*

⁶*Department of Experimental and Specialty Medicine (DIMES),
Division of Radiology S. Orsola – Malpighi Hospital, University of Bologna, Bologna, Italy*



ULTRA-HIPOFRACIONAMENTO

Definitivo



PROTOCOLO DE PLANEJAMENTO SBRT PRÓSTATA

RTOG 0938

DOSE: 5 x 725cGy (36,25Gy)

Próstata (PTV)	<u>D_{máx}</u> (0.03cc)	≤ 38.78 Gy
	Dose em 95% do volume do PTV	≥ 36.25 Gy
	Dose em 100% do volume do PTV	≥ 34.4 Gy

Restrições de Dose:

OAR	RTOG 0938	Planejado
Reto	<1cc = 38,06Gy	<1cc =
	< 3cc = 34,4Gy	< 3cc =
	90% ≤ 32,625Gy	90% =
	80% ≤ 29Gy	80% =
	50% ≤ 18,125Gy	50% =

Resgate

Stereotactic body radiation therapy for locally recurrent prostatic carcinoma after prior therapeutic irradiation: Prostate-specific antigen response, disease-free survival, and toxicity

Donald B. Fuller, MD

Financial relationships to disclose:

Company

Accuray

Varian

Viewray

Nature of Relationship

Honoraria; Research support, Stock ownership

Stock ownership

Stock Ownership

  #ASTRO18

2018 ANNUAL MEETING | HENRY B. GONZALEZ CONVENTION CENTER | SAN ANTONIO



Resgate

Practical Radiation Oncology (2015) 5, e615-e623



Original Report

High-dose-rate stereotactic body radiation therapy for postradiation therapy locally recurrent prostatic carcinoma: Preliminary prostate-specific antigen response, disease-free survival, and toxicity assessment



**Donald B. Fuller MD ^{a,*}, James Wurzer MD, PhD ^b, Reza Shirazi MD ^a,
Stephen S. Bridge MD ^c, Jonathan Law MS ^b, George Mardirossian PhD ^a**

^a*Department of Radiation Oncology, Genesis Healthcare Partners, Inc., San Diego, California*

^b*Department of Radiation Oncology, Atlanticare, Egg Harbor, New Jersey*

^c*Department of Urology, Genesis Healthcare Partners, Inc., San Diego, California*

Received 6 January 2015; revised 4 April 2015; accepted 20 April 2015



ULTRA-HIPOFRACIONAMENTO

Resgate

REPORTS OF PRACTICAL ONCOLOGY AND RADIOTHERAPY 20 (2015) 425–429



Available online at www.sciencedirect.com

ScienceDirect

journal homepage: <http://www.elsevier.com/locate/rpor>



Review

Retreatment for prostate cancer with stereotactic body radiation therapy (SBRT): Feasible or foolhardy?



Stefano Arcangeli^{a,*}, Linda Agolli^b, Vittorio Donato^a

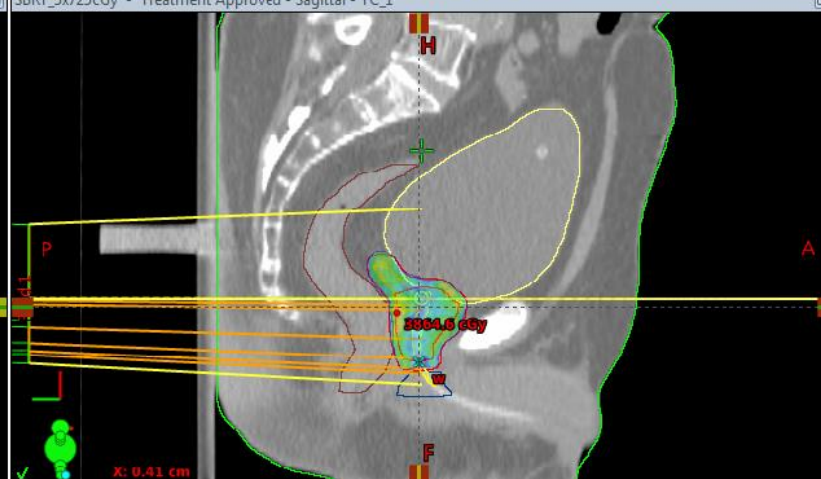
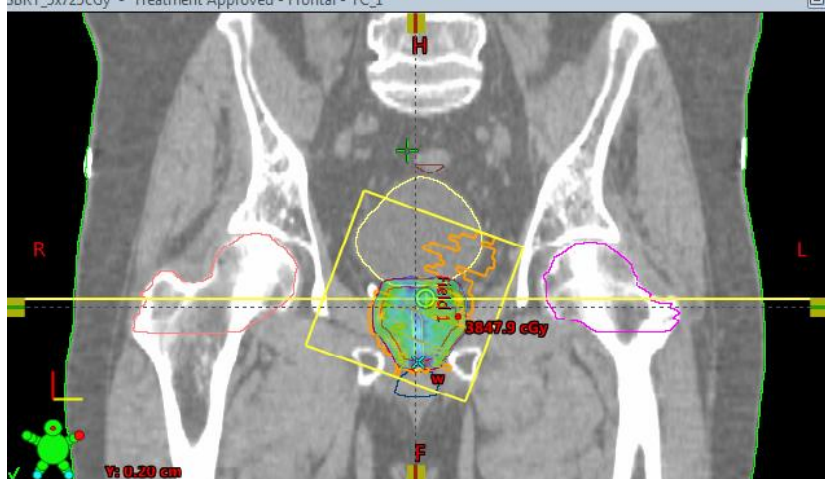
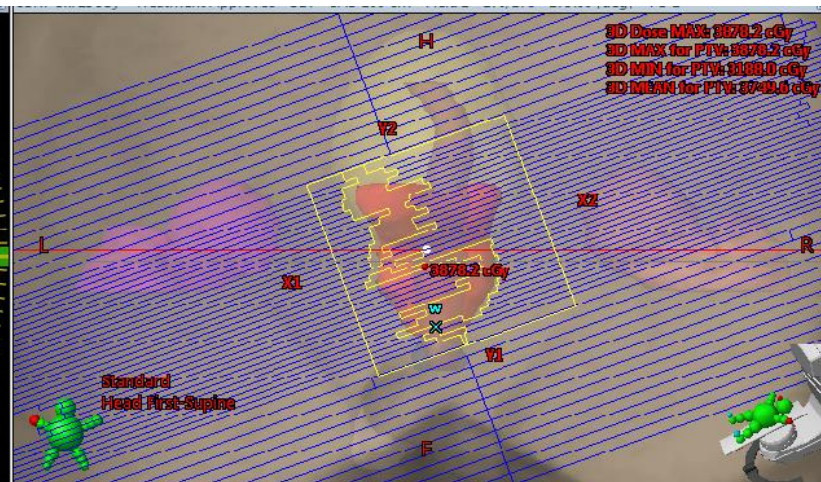
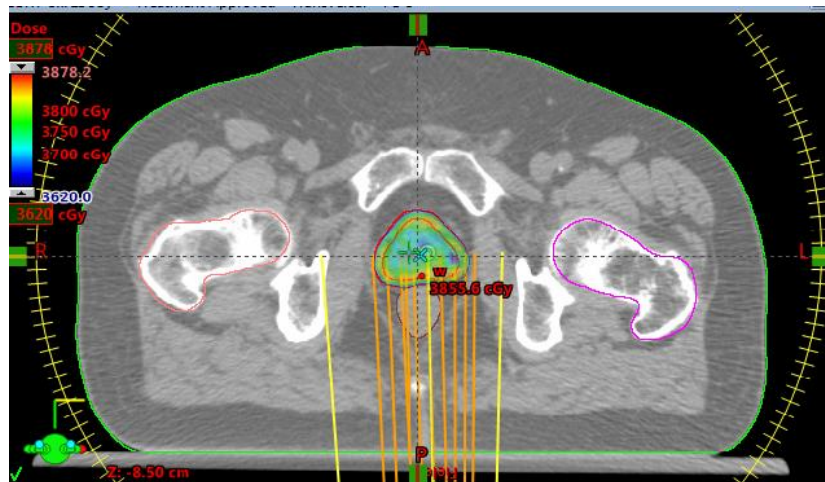
^a Department of Radiotherapy, Azienda Ospedaliera S. Camillo-Forlanini, Rome, Italy

^b Department of Radiotherapy, Azienda Ospedaliera S. Andrea – Facoltà di Medicina e Psicologia dell' Università di Roma "La Sapienza", Rome, Italy



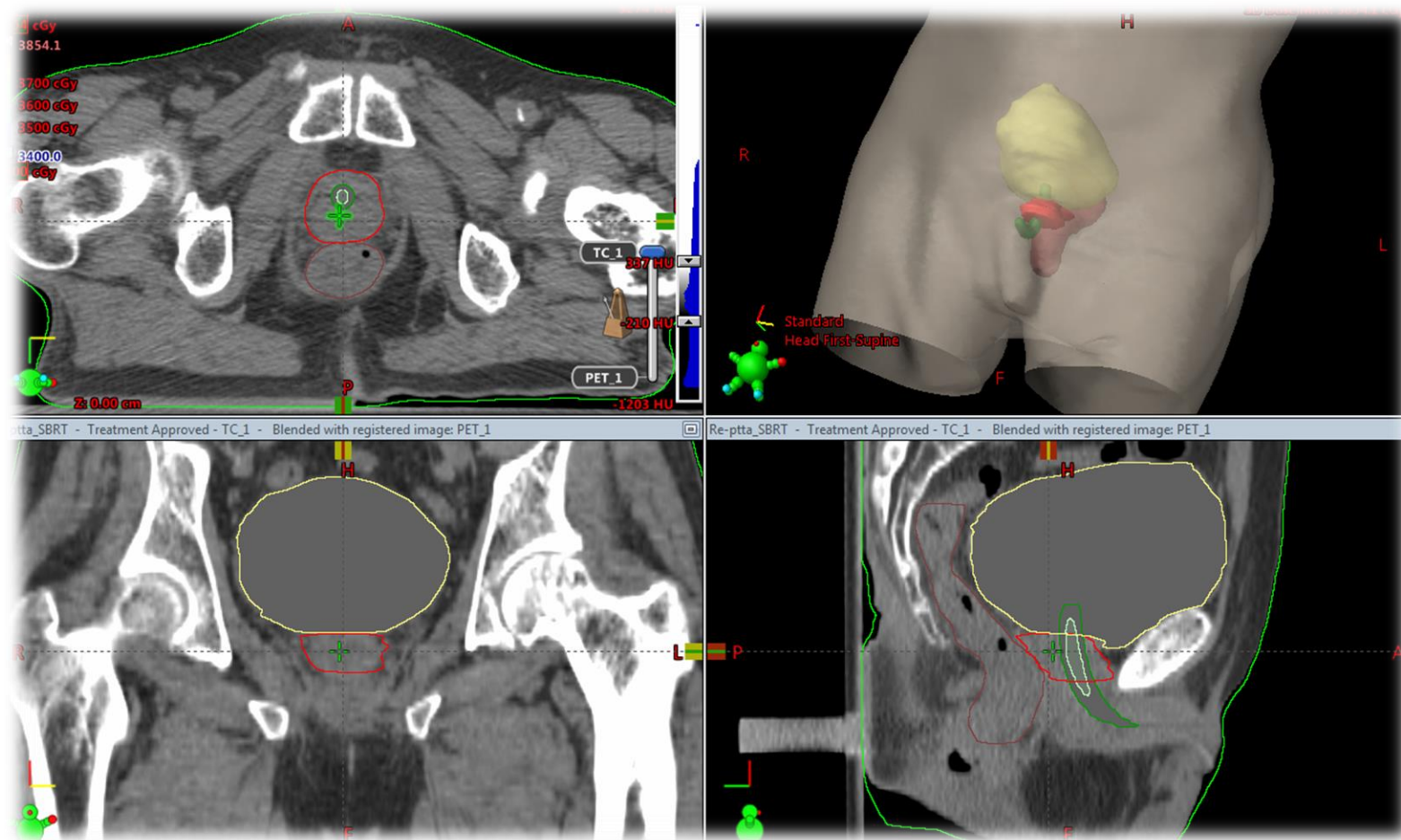
ULTRA-HIPOFRACIONAMENTO

SBRT - definitivo



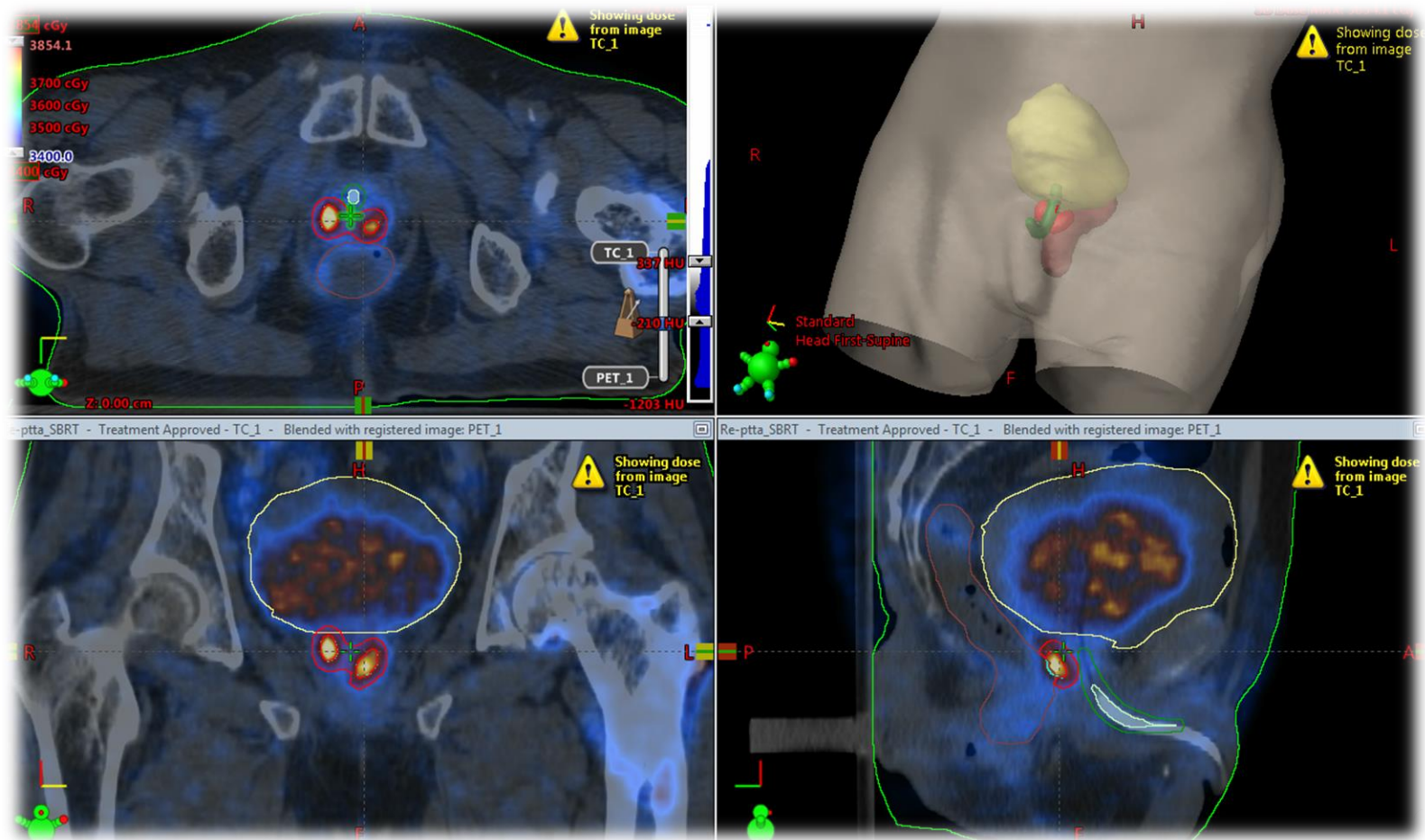
ULTRA-HIPOFRACIONAMENTO

Resgate



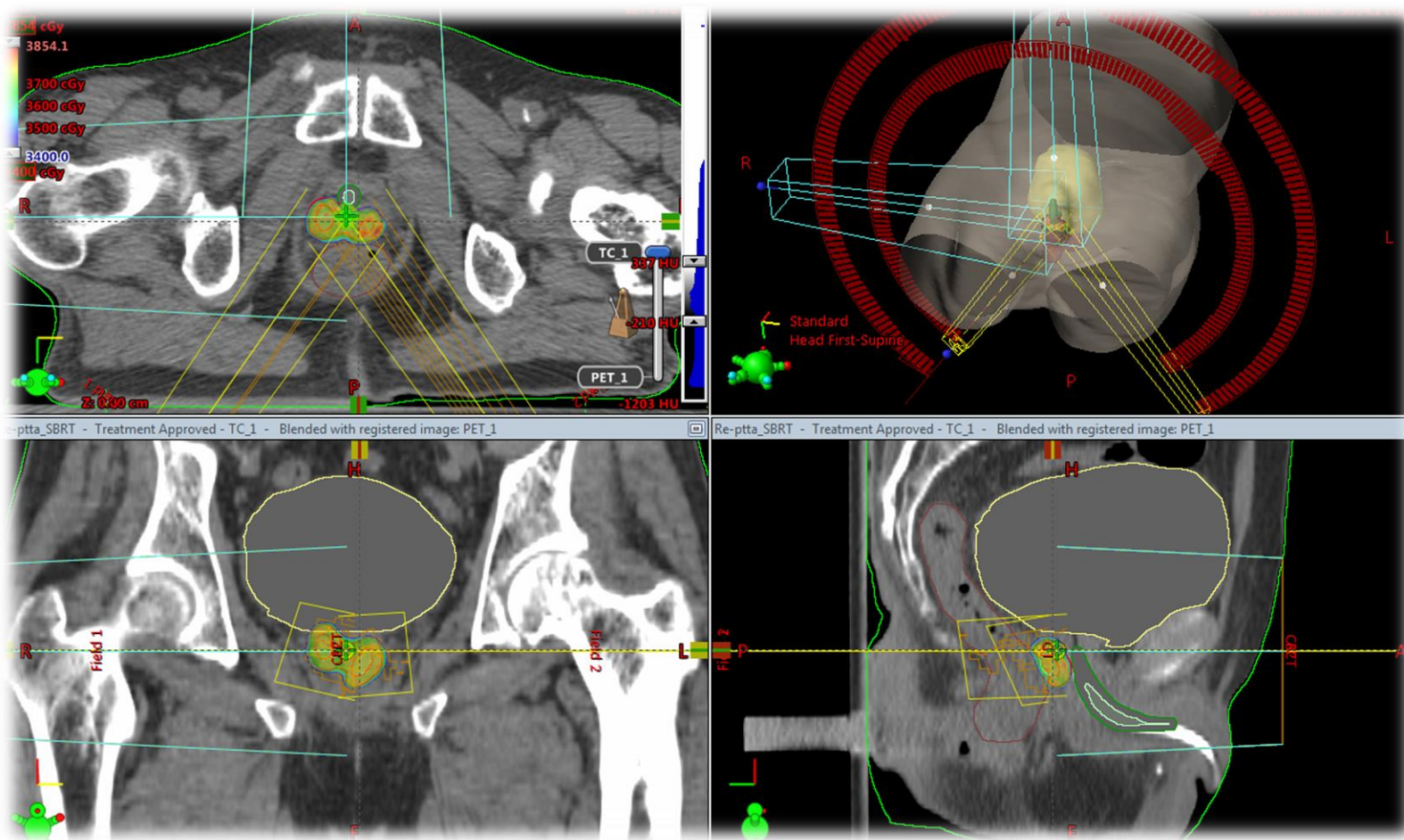
ULTRA-HIPOFRACIONAMENTO

Resgate



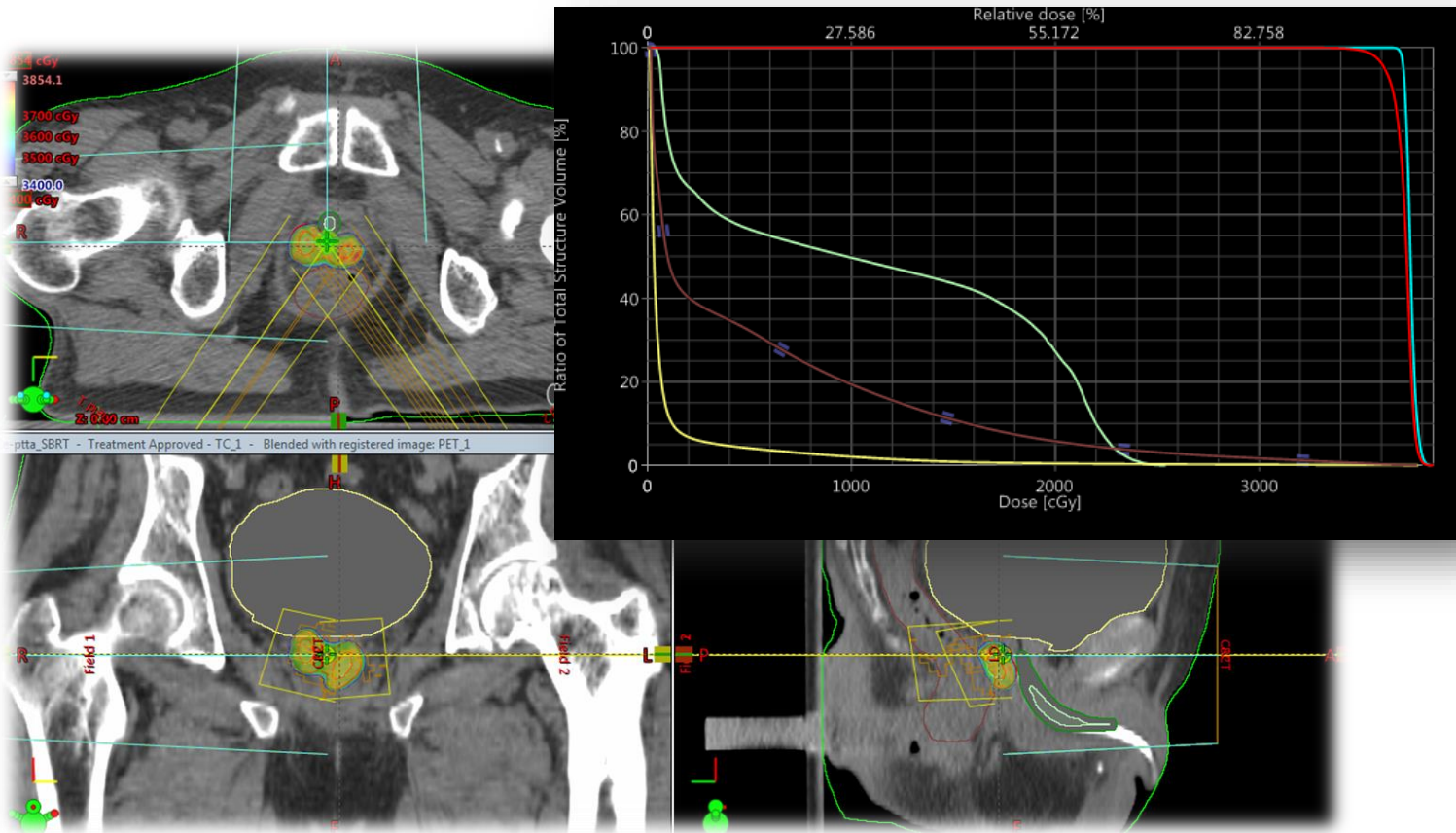
ULTRA-HIPOFRACIONAMENTO

Resgate



ULTRA-HIPOFRACIONAMENTO

Resgate



HIPOFRACIONAMENTO DA PRÓSTATA



Conclusões

- ✓ Tratamento tecnicamente viável, com pouca modificação na rotina de planejamentos
- ✓ Toxicidade aguda GI discretamente maior , tardia idêntica
- ✓ Margens devem ser calculadas de acordo com protocolo de cada instituição
- ✓ Ganho de tempo para o departamento é relevante
- ✓ Tratamento hipofracionado sugerido para maioria = **ASTRO 2018**
- ✓ Recomendado principalmente em instituições públicas / alta demanda
- ✓ Ultra hipofracionamento com indicações ampliadas

