Associazione
Italiana
Radioterapia
Oncologica

Trattamento del carcinoma prostatico a rischio basso-intermedio con modalità BRT-HDR

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NCCN Guidelines Version 4.2013
Prostate Cancer

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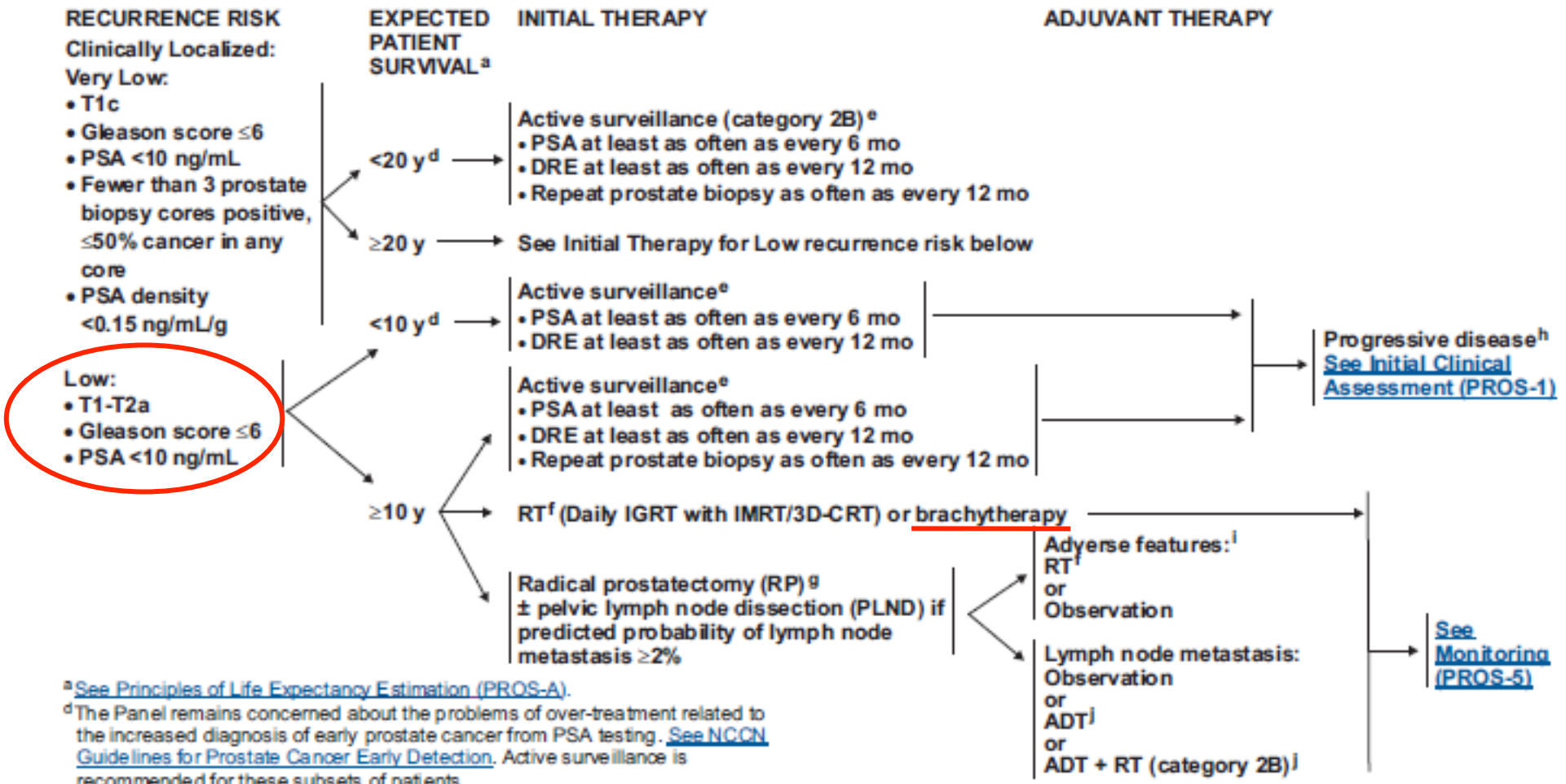
Discussion



[a] See Principles of Life Expectancy Estimation (PROS-A).

[d] The Panel remains concerned about the problems of over-treatment related to the increased diagnosis of early prostate cancer from PSA testing. See NCCN Guidelines for Prostate Cancer Early Detection. Active surveillance is recommended for these subsets of patients.

[e] Active surveillance involves actively monitoring the course of disease with the expectation to intervene if the cancer progresses. See Principles of Active Surveillance (PROS-B).

[f] See Principles of Radiation Therapy (PROS-C).

[g] See Principles of Surgery (PROS-D).

[h] Criteria for progression are not well defined and require physician judgement; however, a change in risk group strongly implies disease progression.

[i] Adverse laboratory/pathologic features include: positive margins, seminal vesicle invasion, extracapsular extension, or detectable PSA.

[j] See Principles of Androgen Deprivation Therapy (PROS-E).

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

American Brachytherapy Society

General Inclusion Criteria:

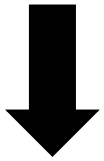
- Clinical Stage
  - T1-T3b and selected T4
- Gleason Score
  - Gleason score 2-10
- PSA
  - No upper limit, but in almost all cases, patient does not have documented distant metastasis (TxN0M0)

Exclusion Criteria:

- Relative Contraindications
  - Severe urinary obstructive symptoms
  - Extensive TURP defect or TURP within 6 month
  - Collagen vascular disease
- Absolute Contraindications
  - Unable to undergo anesthesia (general, spinal, epidural, or local)
  - Unable to lay flat

Scopo dello studio

- Efficacia : riduzione del PSA
- Tossicità GI: RTOG/EORTC
- Tossicita GU:RTOG/EORTC
- Sintomatologia urinaria: IPSS
- QoL



<u>Adenocarcinoma prostatico a basso-intermedio rischio</u>

BRACHITERAPIA HDR

Il trattamento di BRT-HDR (high dose rate, DR>12 Gy/h) si avvale dell'utilizzo di un impianto interstiziale temporaneo di vettori attraverso i quali viene veicolata una sorgente radioattiva di 192Ir.

Vantaggi:

- *Erogazione di dose altamente conformata al target*
- *Rapida caduta di dose con risparmio dei tessuti sani*
- *Somministrazione della dose in un breve intervallo di tempo*
- *Ottimizzazione dose*

The emerging role of high-dose-rate (HDR) brachytherapy as monotherapy for prostate cancer

Yasuo YOSHIOKA[1,*], Ken YOSHIDA[2], Hideya YAMAZAKI[3], Norio NONOMURA[4] and Kazuhiko OGAWA[1]

(Received 22 January 2013; revised 26 February 2013; accepted 2 March 2013)

High-dose-rate (HDR) brachytherapy as monotherapy is a comparatively new brachytherapy procedure for prostate cancer. In addition to the intrinsic advantages of brachytherapy, including radiation dose concentration to the tumor and rapid dose fall-off at the surrounding normal tissue, HDR brachytherapy can yield a more homogeneous and conformal dose distribution through image-based decisions for source dwell positions and by optimization of individual source dwell times. Indication can be extended even to T3a/b or a part of T4 tumors because the applicators can be positioned at the extracapsular lesion, into the seminal vesicles, and/or into the bladder, without any risk of source migration or dropping out. Unlike external beam radiotherapy, with HDR brachytherapy inter-/intra-fraction organ motion is not problematic. However, HDR monotherapy requires patients to stay in bed for 1–4 days during hospitalization, even though the actual overall treatment time is short. Recent findings that the α/β value for prostate cancer is less than that for the surrounding late-responding normal tissue has made hypofractionation attractive, and HDR monotherapy can maximize this advantage of hypofractionation. Research on HDR monotherapy is accelerating, with a growing number of publications reporting excellent preliminary clinical results due to the high 'biologically effective dose (BED)' of >200 Gy. Moreover, the findings obtained for HDR monotherapy as an early model of extreme hypofractionation tend to be applied to other radiotherapy techniques such as stereotactic radiotherapy. All these developments point to the emerging role of HDR brachytherapy as monotherapy for prostate cancer.

Author [ref.]	Dose fractionation	No. of Patients	Follow-up (year)	PSA control rate/ Risk group	Late toxicity ≥ Grade 2[a]	
					Genitourinary	Gastrointestinal
Yoshioka [submitted for publication, 21]	54 Gy/9 Fr.	112	5.4	85% (5y)/Low 93% (5y)/Intermediate 79% (5y)/High	7.1%	7.1%
	45.5 Gy/7 Fr.	63	3.5	96% (3y)/Intermediate 90% (3y)/High	6.3%	1.6%
Demanes [12]	42 Gy/6 Fr.	157	5.2	97% (5y)/Low–intermediate	28.9%	<1.0%
Martinez [18, 22]	38 Gy/4 Fr.	171	4.6	91% (5y)/Low–intermediate	40.5%	2.0%
	24 Gy/2 Fr.	50	1.4	Not available	25.5%	5.3%
	27 Gy/2 Fr.	44				
Rogers [11]	39 Gy/6 Fr.	284	2.7	94% (5y)/Intermediate	7.7%	0.0%
Zamboglou [10]	38 Gy/4 Fr.	141	4.4	95% (5y)/Low	27.5%	2.6%
	38 Gy/4 Fr.	351		93% (5y)/Intermediate		
	34.5 Gy/3 Fr.	226		93% (5y)/High		
Hoskin [9]	34 Gy/4 Fr.	34	3.5	95% (3y)/Intermediate	33.0%	13.0%
	36 Gy/4 Fr.	25		87% (3y)/High	40.0%	4.0%
	31.5 Gy/3 Fr.	55			34.0%	7.0%
Ghadjar [13]	38 Gy/4 Fr.	36	3	100% (3y)/Low–intermediate	36.1%	5.6%
Barkati [14]	30 Gy/3 Fr.	19	3.3	88% (3y)/Low–intermediate	59.0%	5.1%
	31.5 Gy/3Fr.	19				
	33 Gy/3 Fr.	19				
	34.5 Gy/3 Fr.	22				
Komiya [16]	45.5 Gy/7 Fr.	51	1.4	100% (2y)/Low–high	11.8%	2.0%
Prada [17]	19 Gy/1 Fr.	40	1.6	100% (2.7y)/Low 88% (2.7y)/Intermediate	0.0%	0.0%

HDR = high-dose-rate, PSA = prostate-specific antigen, Fr. = fraction(s). [a]Scored per event not per patient.

Criteri di inclusione

- **conferma istologica;**
- **assenza di meta. ossee assenza di malattie psichiatriche;**
- **I.K. ≥ 60;**
- **non sottoposti a prostatectomia radicale;**
- **assenza di limitazioni funzionali dell'articolazione coxofemorale;**
- **PFR > 10 ml/sec;**
- **IPSS < 20;**
- **Vol. prostatico < 60 cc;**
- **No comorbidità (elevato rischio anestesiologico);**

Materiali e Metodi

Aprile 2011-Dicembre 2012 ⇨ 15 pazienti

Età media : 65 anni (58-77 aa)

Stadio clinico:

T1c: 12 pz
T2a: 3 pz

PSA medio esordio: 5,98 ng/mL (2,71-9 ng/mL)

Gleason Score:

3+3 = 6 : 9 pz
3+4 = 7 : 6 pz

Volume ecografico medio: 30 cc (11-40 cc)

Valutazione preliminare

- Dosaggio PSA
- Ecografia prostatica T.R.
- TC per valutazione arco pubico
- Flussimetria urinaria

- Esami ematochimici di routine
- Rx torace
- ECG
- Consulenza anestesiologica

- Toilette intestinale il giorno precedente, sospensione di eventuali terapie anticoagulanti e antiaggreganti 3 giorni prima del trattamento.

15 pazienti

12 pz : 2 fr di BR
(intervallo interf
Deq.=124,0 Gy c

ELSEVIER

Brachytherapy

Volume 11, Issue 2, March–April 2012, Pages 105–110

High-dose-rate interstitial brachytherapy as monotherapy in one fraction and transperineal hyaluronic acid injection into the perirectal fat for the treatment of favorable stage prostate cancer: Treatment description and preliminary results

Pedro J. Prada[1], Isabel Jimenez[1], Herminio González-Suárez[1], José Fernández[2], Covadonga Cuervo-Arango[1], Lucia Mendez[1]

PURPOSE: To evaluate the technical feasibility, acute and late genitourinary (GU) toxicity, and gastrointestinal toxicity after high-dose-rate (HDR) brachytherapy as monotherapy in one fraction with transperineal hyaluronic acid injection into the perirectal fat to displace the rectal wall away from the radiation sources to decrease rectal toxicity.

METHODS AND MATERIALS: Between April 2008 and January 2010, 40 consecutive patients were treated with favorable clinically localized prostate cancer; the median followup was 19 months (range, 8-32). No patients received external beam radiation, and 35% received hormone therapy before brachytherapy. All patients received one implant and one fraction of HDR. Fraction dose was 19 Gy. Toxicity was reported according to the Common Toxicity Criteria for Adverse Event, Version 4.0.

RESULTS: All patients tolerated the implantation procedure very well with minimal discomfort. No intraoperative or perioperative complications occurred. Acute toxicity Grade 2 or more was not observed in any patients. No chronic toxicity has been observed after treatment. Logistic regression showed that the late Grade 1 GU toxicity was associated with D(90) (p=0.050). The 32-month actuarial biochemical control was 100% and 88%, respectively (p=0.06) for low- and intermediate-risk groups.

CONCLUSIONS: This is the first published report of the use of HDR brachytherapy as monotherapy in one fraction for patients with favorable-risk prostate cancer. This protocol is feasible and very well tolerated with low GU morbidity, no gastrointestinal toxicity, and the same level of low-dose-rate biochemical control at 32 months.

Dose Contraints 14 Gy/2 fr

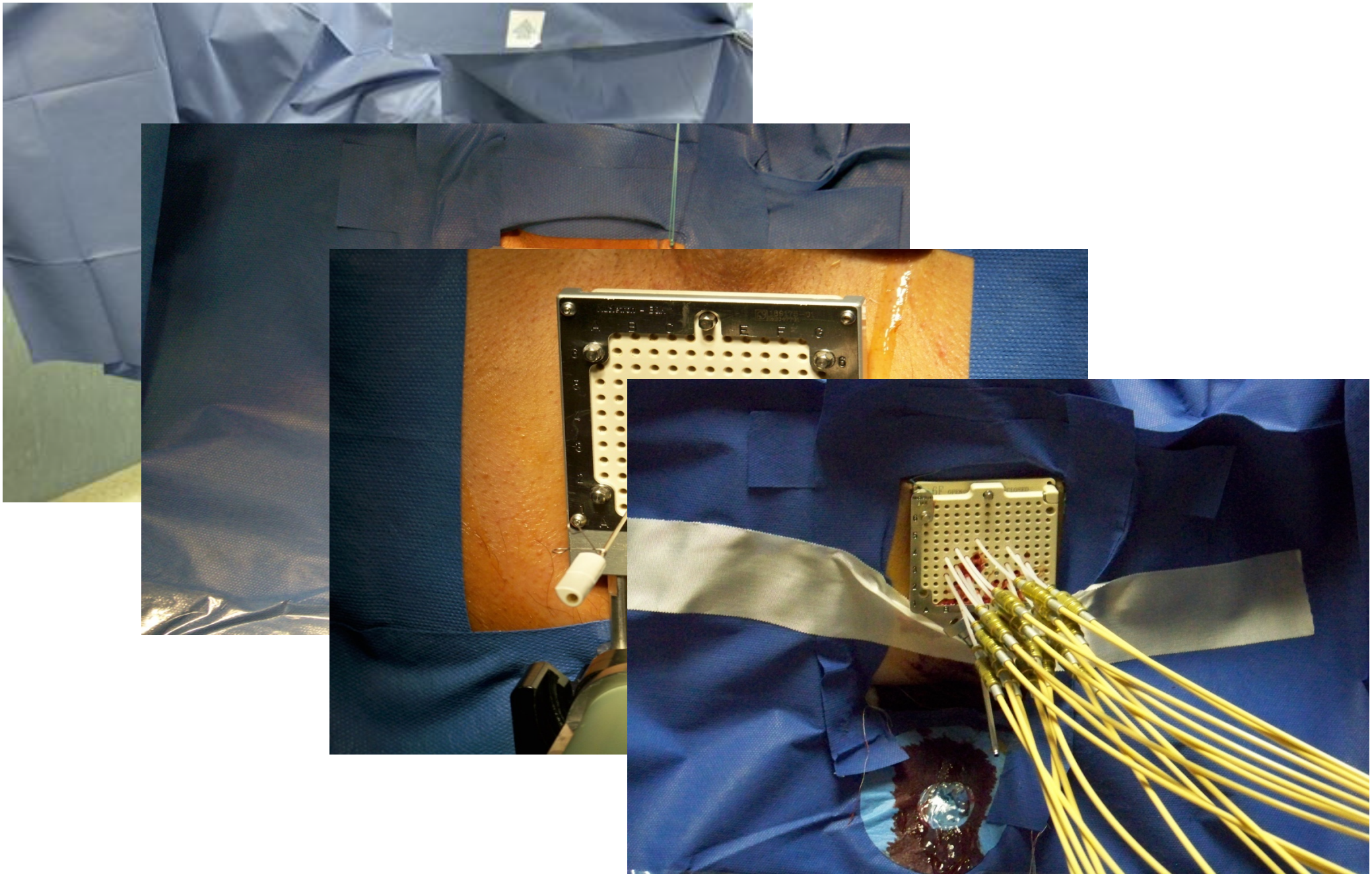
TARGET	V 100	> 95 % DP
	V 125 V 150	< 60 % DP < 30 % DP
URETRA	1 cc	≤ 115 % DP
RETTO	1 cc	≤ 75% DP
VESCICA	1 cc	≤ 75% DP

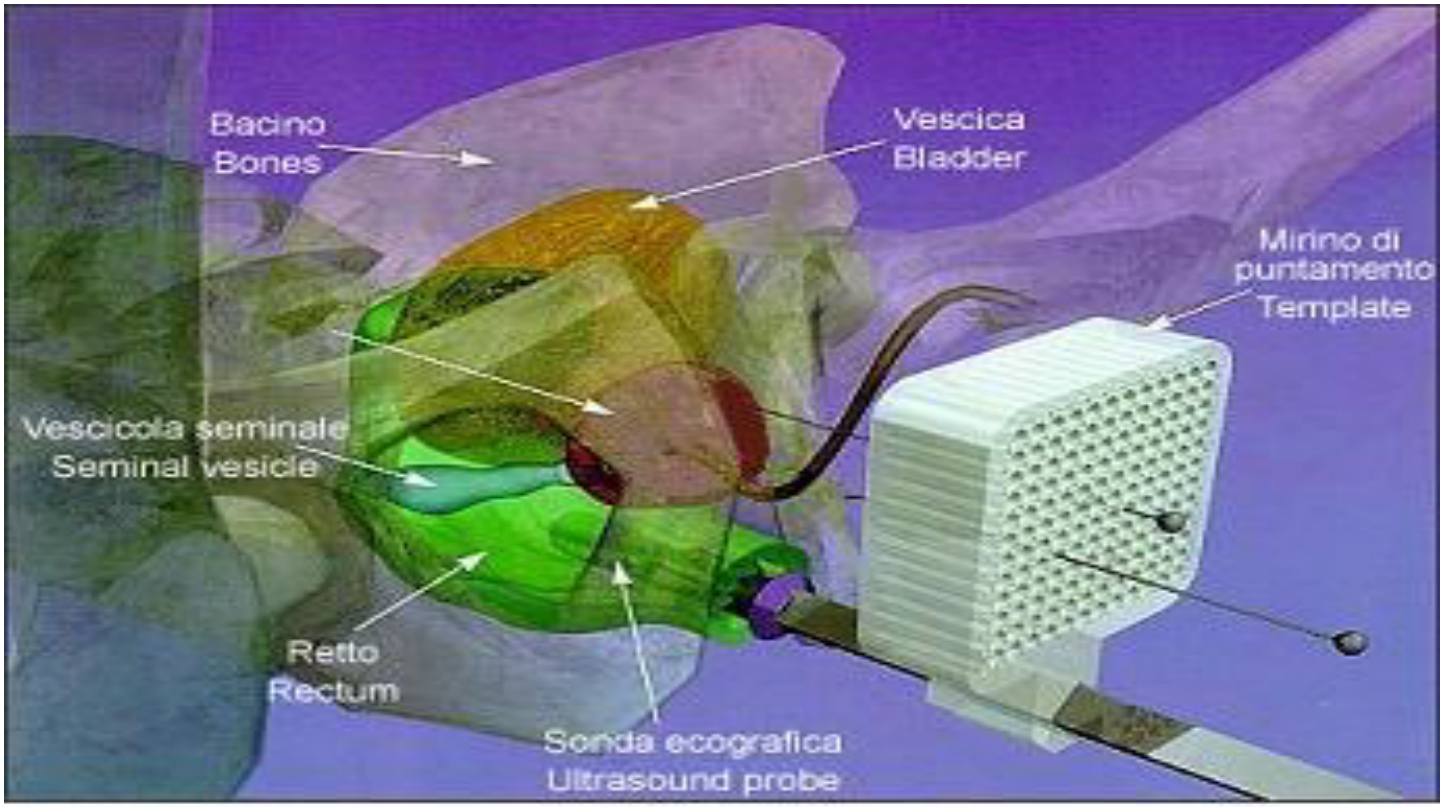
N° Aghi : 14-18 in base al volume prostatico
3-4 mm dall'uretra

Dose Contraints 19 Gy/1 fr

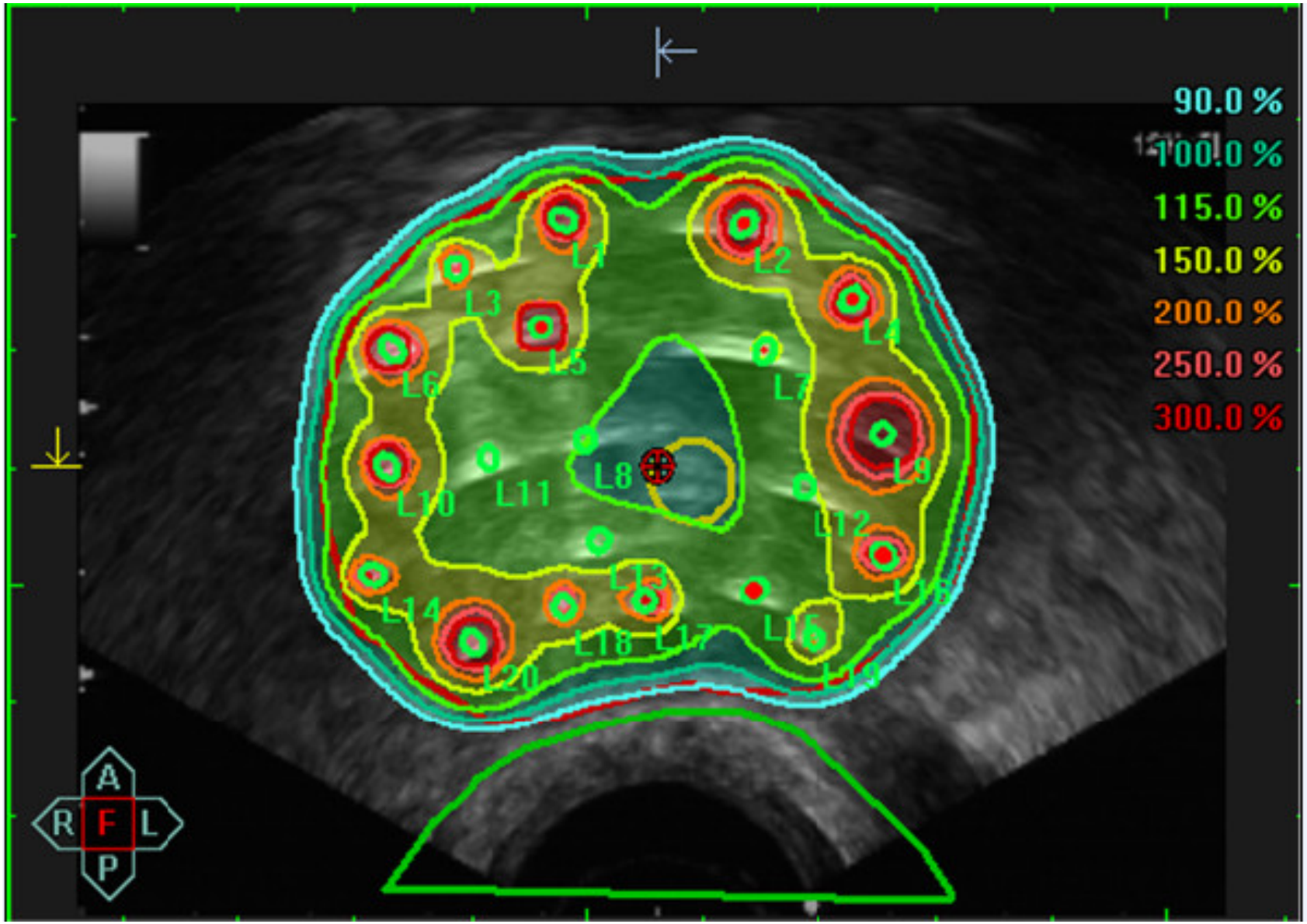
TARGET	V 100	> 90 % DP
	V 125 V 150	< 60 % DP < 30 % DP
URETRA	V100	< 90 % DP
RETTO	2 cc	< 75% DP
VESCICA	2 cc	< 80% DP

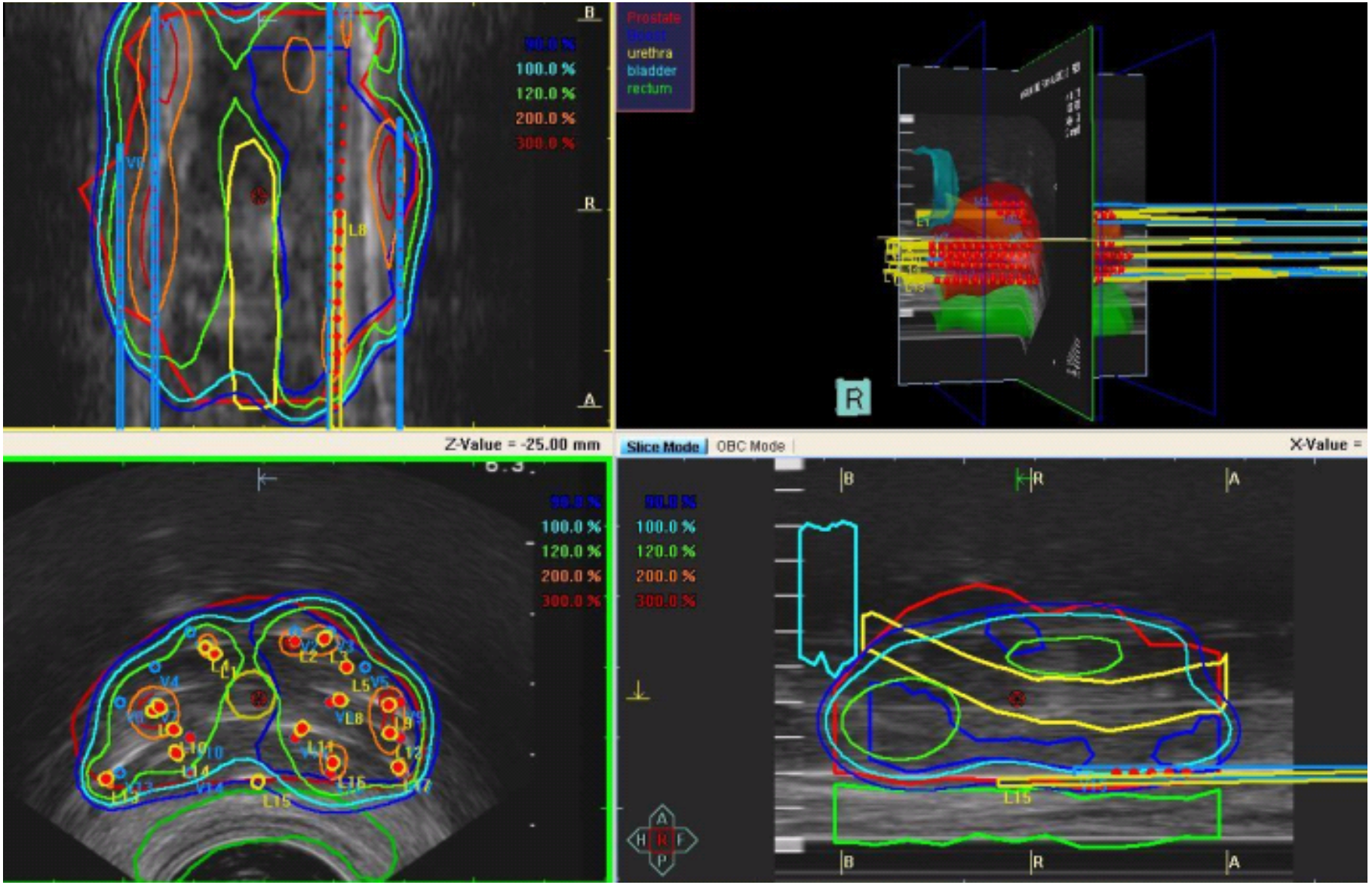
N° Aghi : 14-18 in base al volume prostatico
3-4 mm dall'uretra





Dispositivo di puntamento per impianto ecoguidato
Template for ultrasound guided implant

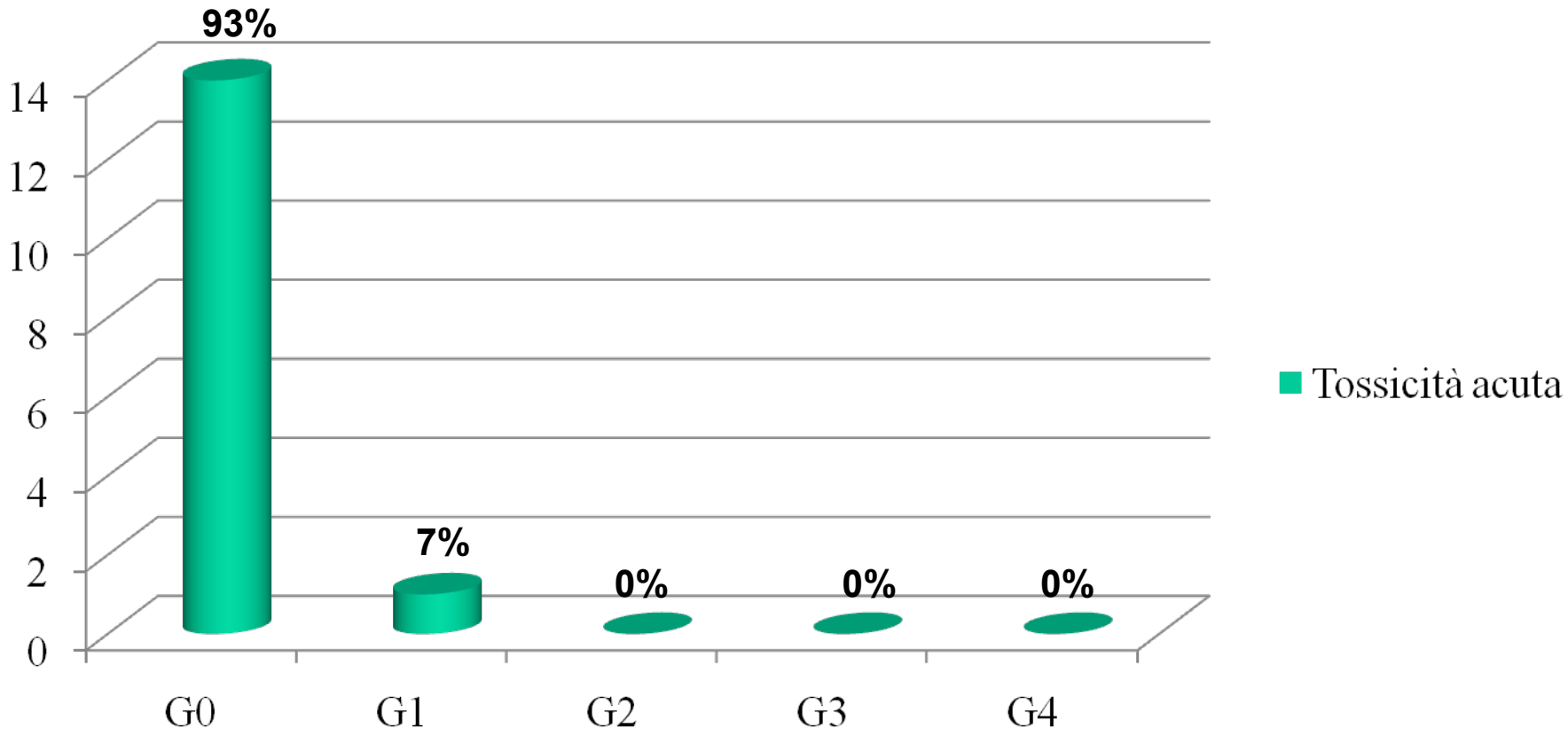

90.0 %
100.0 %
115.0 %
150.0 %
200.0 %
250.0 %
300.0 %
L1
L2
L3
L4
L5
L6
L7
L8
L9
L10
L11
L12
L13
L14
L15
L16
L17
L18
L19
L20
A
R
F
L
P


B
R
A
100.0 %
120.0 %
200.0 %
300.0 %
L8
Prostate
urethra
bladder
rectum
R
Z-Value = -25.00 mm
Slice Mode
OBC Mode
X-Value =
L15

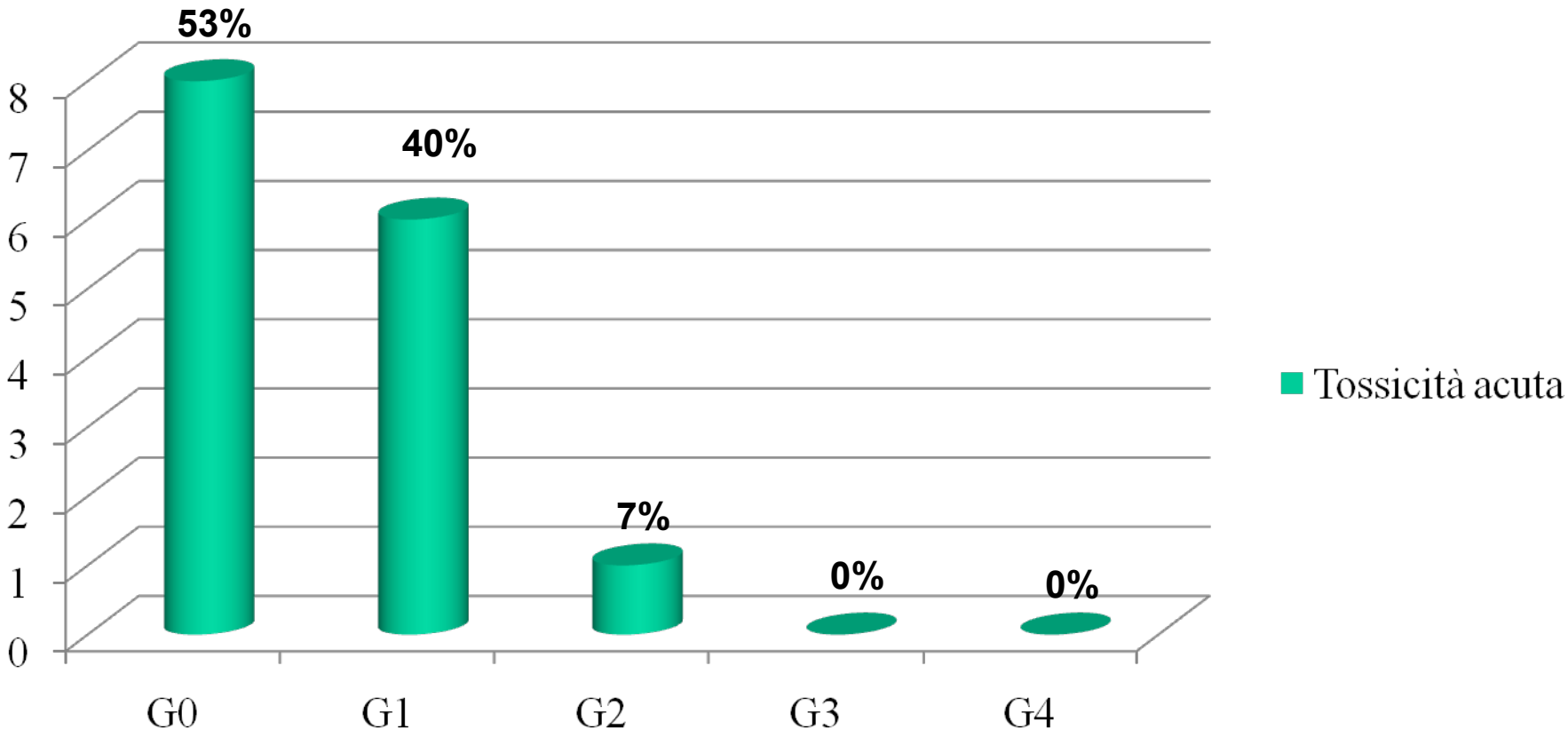
Termine del Trattamento

- Compressione emostatica in zona perineale
- Applicazione di ghiaccio per ridurre l'edema
- Lavaggi vescicali
- Cistoclisi continua per 24 h
- Somministrazione di antidolorifici e antibiotici
- Il Pz. in assenza di complicanze viene dimesso il giorno seguente con la seguente terapia:
- Tachipirina 1 gr x 3/die per 4-5 gg
- Ciproxin 500 mg 1cp x 2/die per 3-4 gg

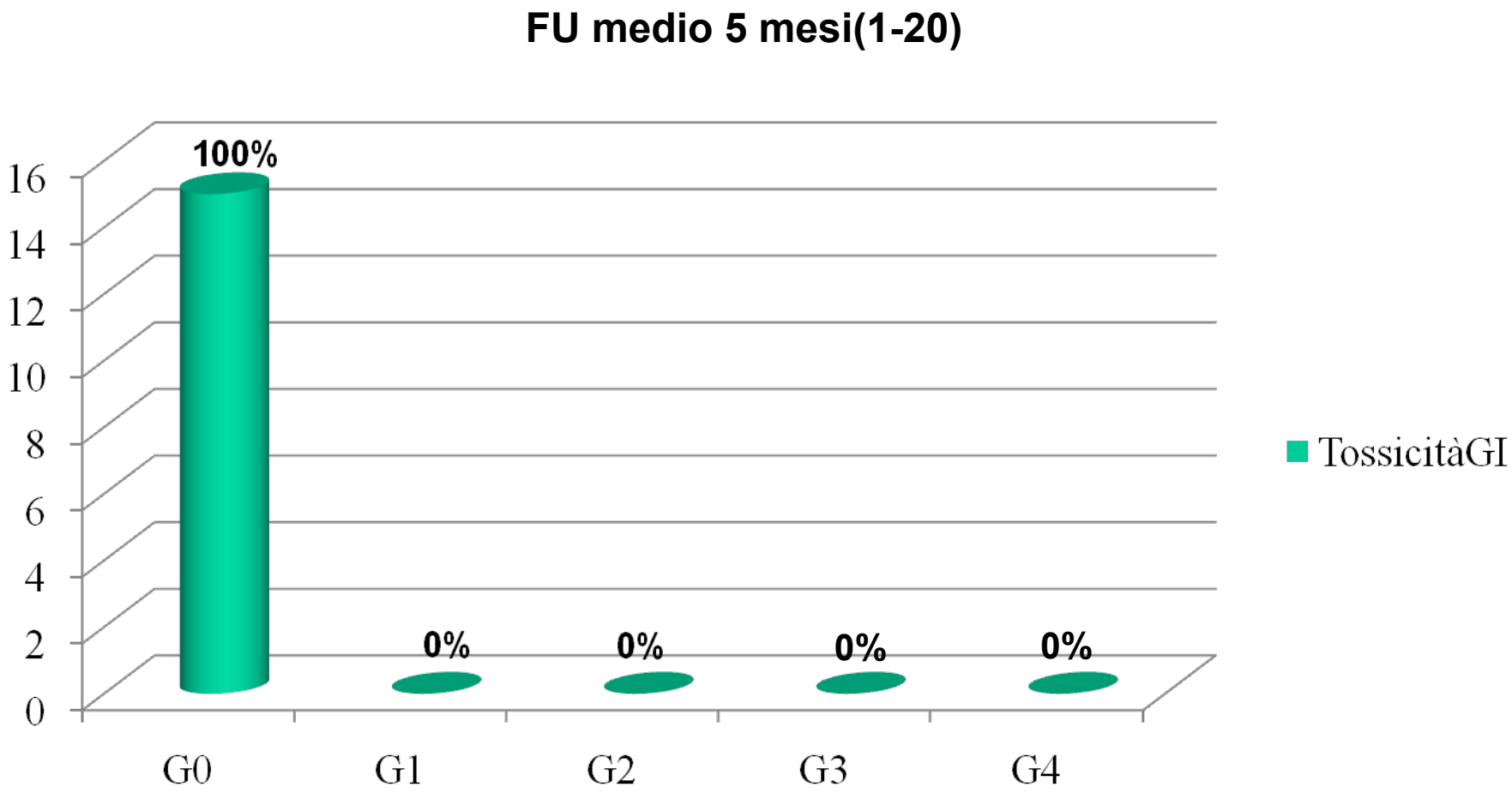
Tossicità acuta GI



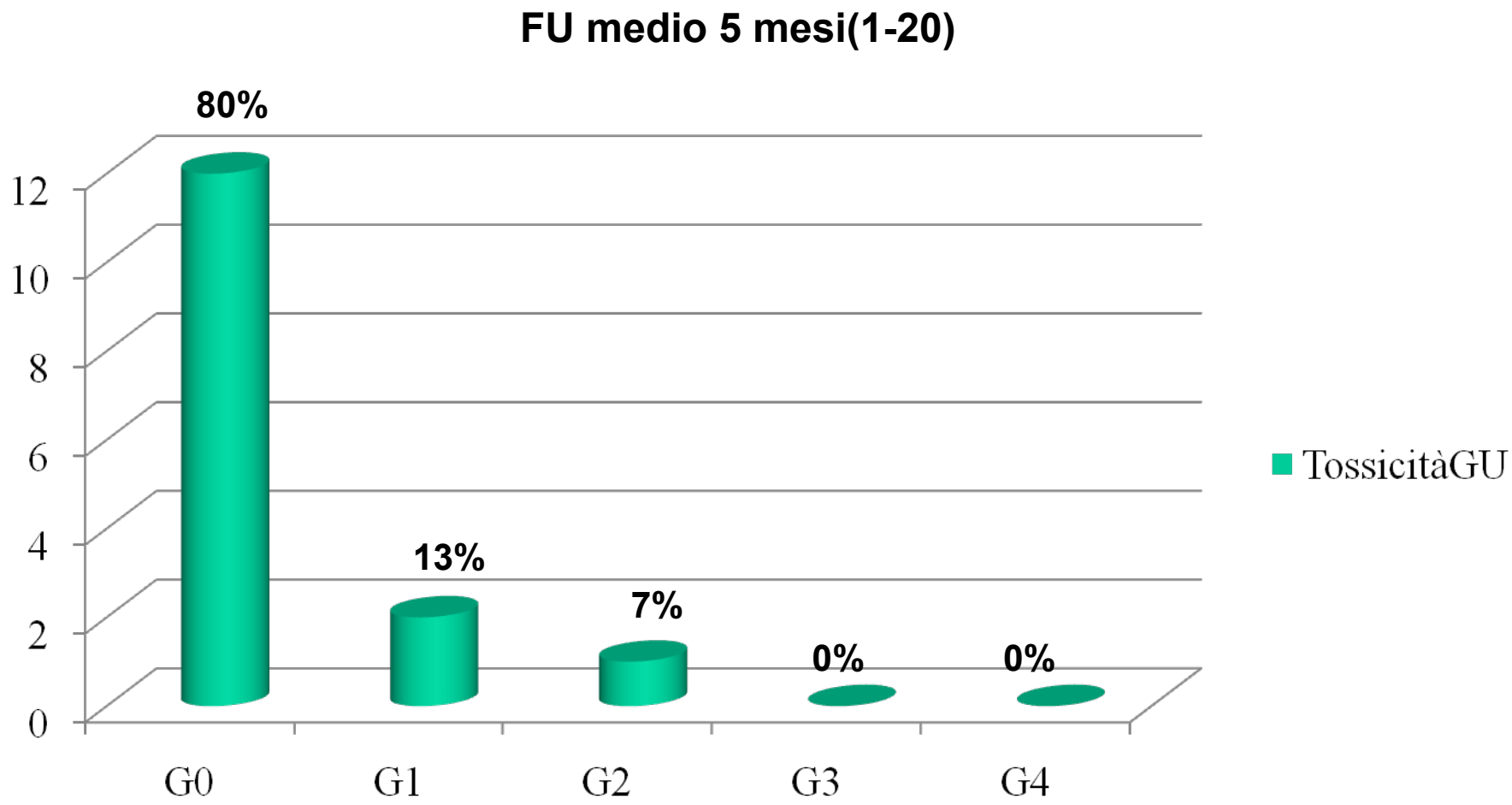
Tossicità acuta GU



Tossicità cronica……..?



Tossicità cronica……..?



High-Dose-Rate Brachytherapy as Monotherapy Delivered in Two Fractions Within One Day for Favorable/Intermediate-Risk Prostate Cancer: Preliminary Toxicity Data

Michel Ghilezan, M.D., Ph.D., Alvaro Martinez, M.D., Gary Gustason, M.D., Daniel Krauss, M.D., J. Vito Antonucci, M.D., Peter Chen, M.D., James Fontanesi, M.D., Michelle Wallace, R.N., Hong Ye, M.S., Alyse Casey, R.N., Evelyn Sebastian, B.S., Leonard Kim, M.S., Amy Limbacher, B.S.

Department of Radiation Oncology, William Beaumont Hospital and Rose Cancer Institute, Royal Oak, Michigan

Favorable-risk prostate cancer patients treated with a single implant HDR-BT to 24–27 Gy in two fractions within 1 day have excellent tolerance with minimal acute and chronic toxicity. Longer follow-up is needed to confirm these encouraging early results.

the study population for this preliminary report. All patients had clinical Stage T2b or less (American Joint Committee on Cancer, 5th edition), Gleason score 6-7 (3+4), and prostate-specific antigen level of ≤12 ng/mL. Ultrasound-guided HDR-BT with real-time dosimetry was used. The prescription dose was 24 Gy for the first 50 patients and 27 Gy thereafter. The dosimetric goals and constraints were the same for the two dose groups. Toxicity was scored using the National Cancer Institute Common Terminology Criteria for Adverse Events, version 3. The highest toxicity scores encountered at any point during follow-up are reported.

Results

The median follow-up was 17 months (range, 6–40.5). Most patients had Grade 0-1 acute toxicity. The Grade 2 acute genitourinary toxicity was mainly frequency/urgency (13%), dysuria (5%), hematuria, and dribbling/hesitancy (2%). None of the patients required a Foley catheter at any time; however, 8% of the patients experienced transient Grade 1 diarrhea. No other acute gastrointestinal toxicities were found. The most common chronic toxicity was Grade 2 urinary frequency/urgency in 16% of patients followed by dysuria in 4% of patients; 2 patients had Grade 2 rectal bleeding and 1 had Grade 4, requiring laser treatment.

QUESTIONARIO IPSS (International Prostatic Symptoms Score)

Il questionario IPSS, unico questionario validato in lingua italiana per questa patologia, permette una valutazione oggettiva della sintomatologia urinaria del paziente affetto da ipertrofia prostatica.

	Nessuna volta	Meno di una volta su 5	Meno della metà delle volte	Circa la metà delle volte	Più della metà delle volte	Quasi sempre
Quante volte nell'ultimo mese ha avvertito un senso di incompleto svuotamento vescicole al termine della minzione?	0	1	2	3	4	5
Nell'ultimo mese quante volte ha urinato meno di due ore dopo l'ultima minzione?	0	1	2	3	4	5
Nell'ultimo mese Le è mai capitato di dover mingere in più tempi?	0	1	2	3	4	5
Nell'ultimo mese quante volte ha avuto difficoltà a posporre la minzione?	0	1	2	3	4	5
Nell'ultimo mese quanto spesso il getto urinario Le è parso debole?	0	1	2	3	4	5
Quante volte nell'ultimo mese ha dovuto sforzarsi per iniziare ad urinare?	0	1	2	3	4	5
Nel corso dell'ultimo mese, quante volte si è alzato per andare ad urinare la notte?	0	1	2	3	4	5

PUNTEGGIO TOTALE =

Punteggio totale:
0-7 sintomatologia lieve
8-19 sintomatologia moderata
20-35 sintomatologia severa

INDICE DELLA QUALITA' DELLA VITA

	Bene	Soddisfatto	Abbastanza soddisfatto	Così Così	Relativamente Insoddisfatto	Male	Molto male
Se dovesse trascorrere il resto della Sua vita con la Sua attuale condizione urinaria, come si sentirebbe?	0	1	2	3	4	5	6

IPSS pre-trattamento medio = 10

IPSS post-trattamento medio = 8

QoL pre-trattamento medio = 1.45

QoL post-trattamento medio = 1.18

PSA DIAGNOSI ng/mL	PSA FOLLOW-UP ng/ml	RIDUZIONE% del PSA
5,71	6,24	-9,28
7,50	1,00	86,67
5,21	1,38	73,51
8,00	2,35	70,63
8,75	1,00	88,57
2,71	0,68	74,91
9,00	1,44	84,00
3,01	3,00	0,33
4,23	1,60	62,17
3,50	0,45	87,14
6,46	3,42	47,06
6,31	3,00	52,46
5,09	4,02	21,02
3,50	0,49	86,00
8,33	5,27	36,73
5,82	2,36	57,42

93,4% pz.

p=0.004

FU medio 5 mesi(1-20) : fallimento biochimico + 2 ng/ml dal nadir

American Brachytherapy Society consensus guidelines for high-dose-rate prostate brachytherapy

Yoshiya Yamada[1,*], Leland Rogers[2], D. Jeffrey Demanes[3], Gerard Morton[4], Bradley R. Prestidge[5], Jean Pouliot[6], Gil'ad N. Cohen[7], Marco Zaider[7], Mihai Ghilezan[8], I-Chow Hsu[6]

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[6]*Department of Radiation Oncology, Helen Diller Family Comprehensive Cancer Center, San Francisco, CA*
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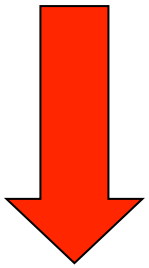
ABSTRACT

delivery are of paramount importance. Despite a wide variation in prescribed doses, the outcomes are highly favorable; no one optimal dose fractionation schedule or normal tissue tolerance criteria can be recommended. Nonetheless, with a multitude of studies reporting long-term results with excellent tumor control and a favorable side-effect profile, HDR brachytherapy is now an established and important treatment for prostate cancer.

control, even for high-risk disease, with low morbidity. HDR monotherapy, both for primary treatment and salvage, are promising treatment modalities.

Conclusioni



Fattibilità

Efficacia

Sicurezza


Grazie per l’attenzione