

XXIII CONGRESSO
AIRO2013

Giardini Naxos - Taormina, 26 - 29 ottobre

**Terapia di supporto in
radioterapia oncologica:
Distretto pelvico**

Regione Siciliana - Assessorato Regionale dei Beni Culturali e dell'Identità Siciliana.
Dipartimento dei Beni Culturali e dell'Identità Siciliana.
Servizio Museo Interdisciplinare Regionale "A. Pepoli" Trapani.



Maria Antonietta Gambacorta

Università Cattolica del Sacro Cuore.

Roma

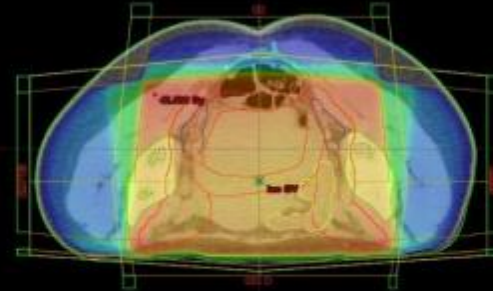
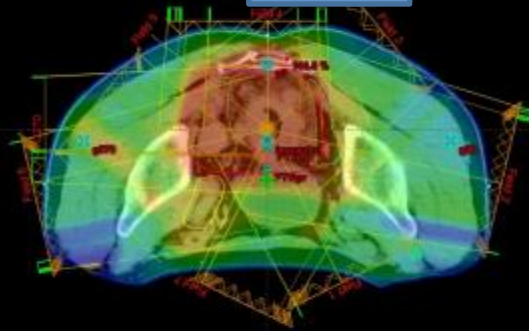
Radioterapia nel distretto pelvico



50 Gy

55 Gy

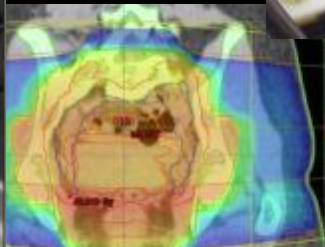
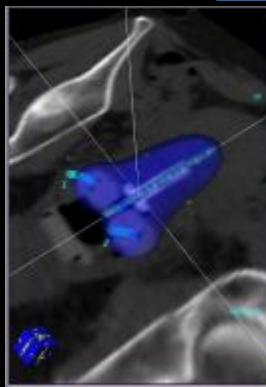
65 Gy



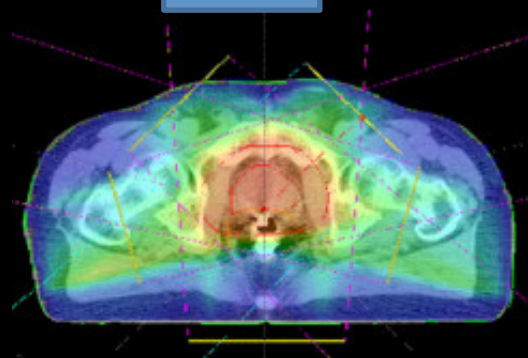
45



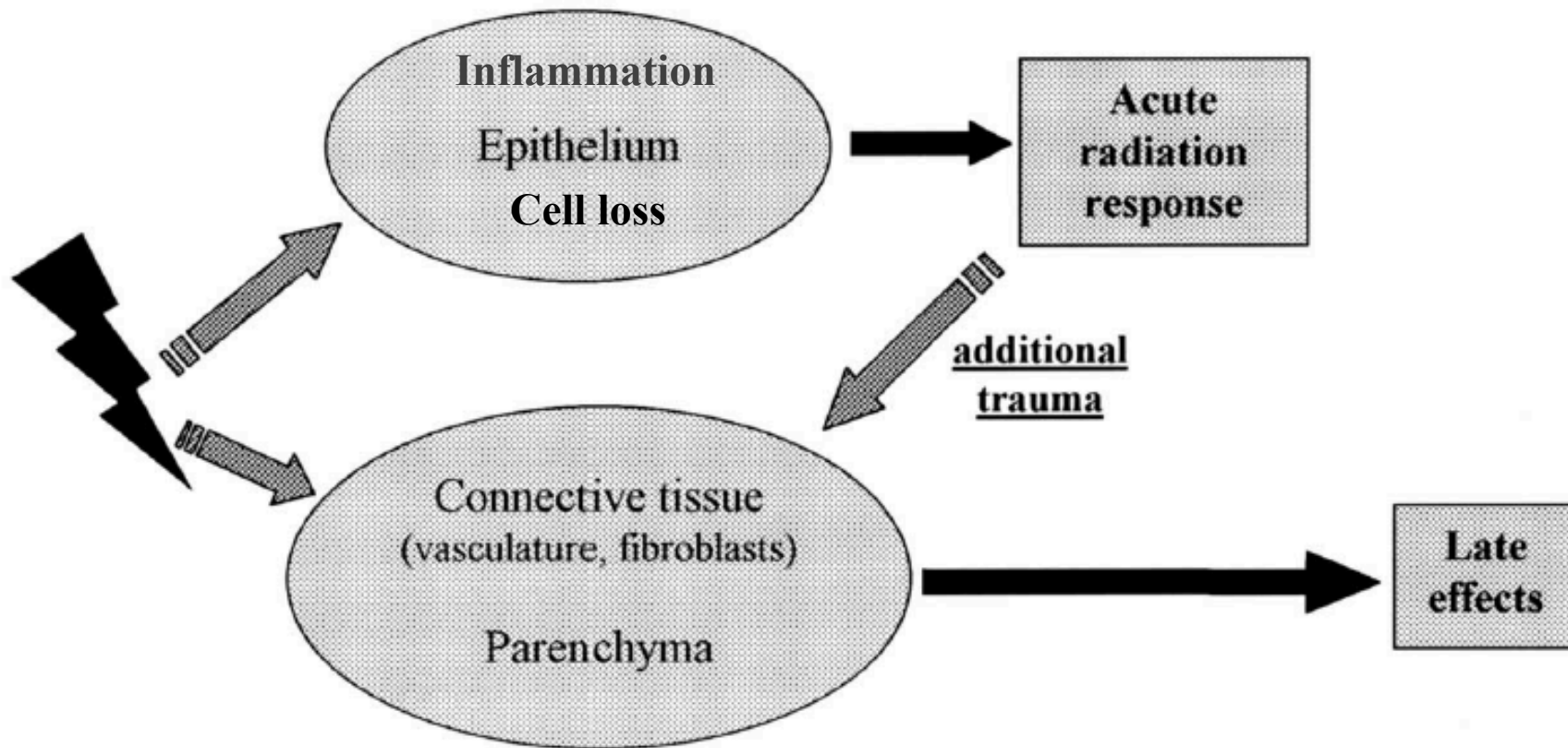
80



85 + Gy

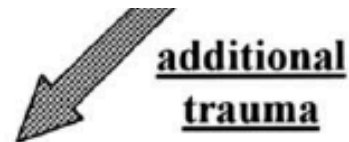
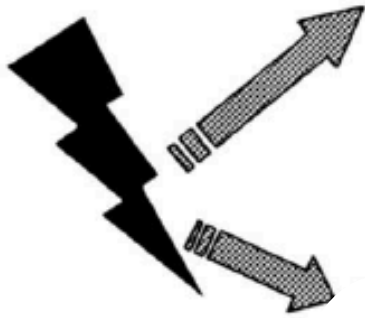


Patogenesisi



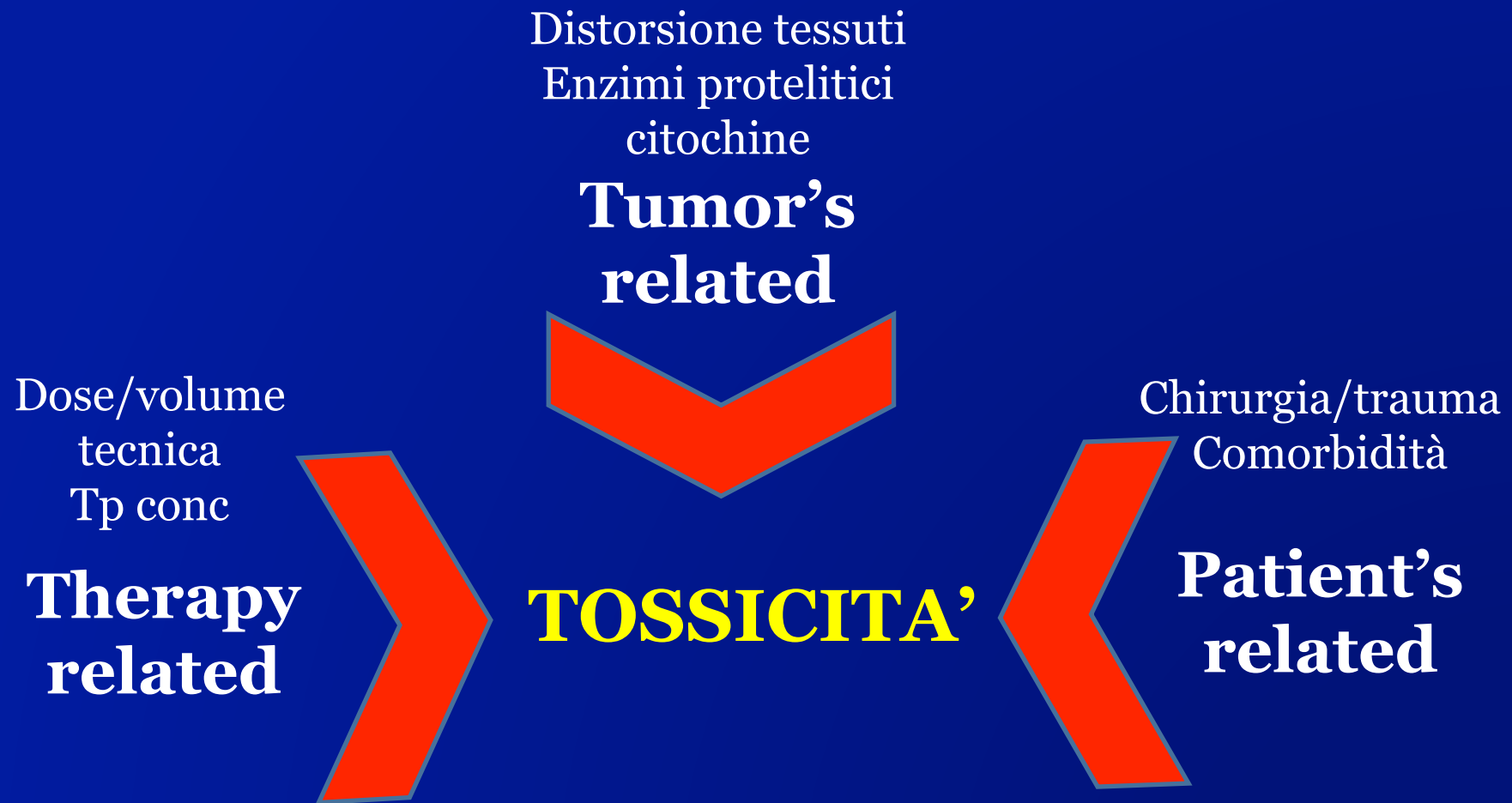
Patogenesi

ACUTE: **inflammation**
cell loss



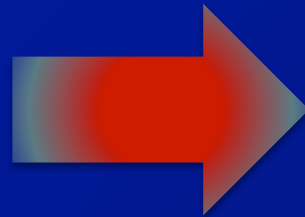
CRONIC:
endoarteritis-hypoxia-fibrosis

Fattori Predisponenti



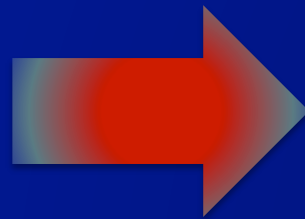
TOSSICITA'

ACUTA



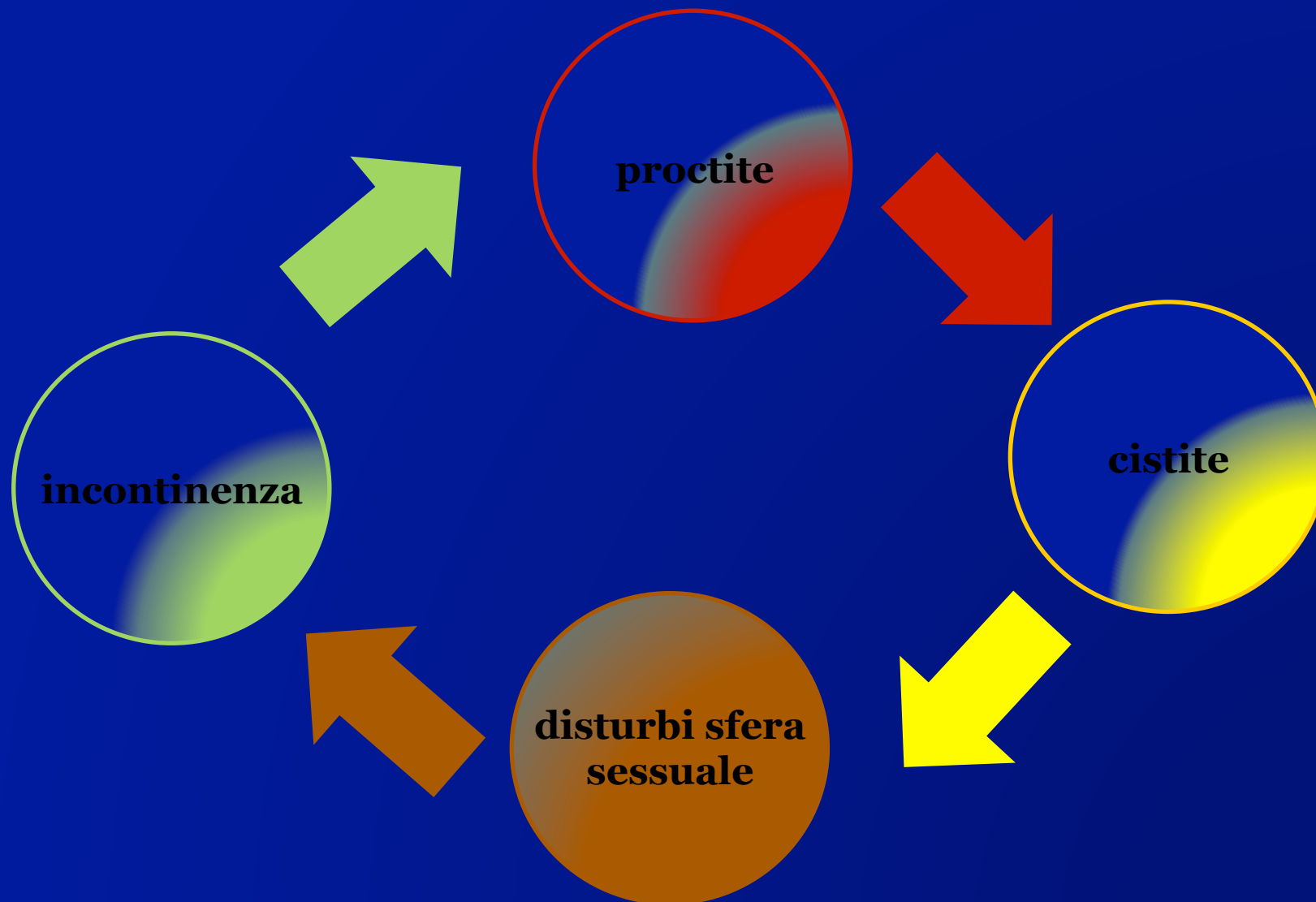
**EFFICACIA
TERAPIA
interruzioni**

CRONICA

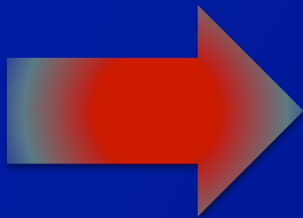


**QUALITA'
di
VITA**

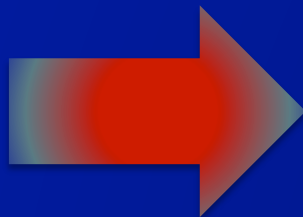
TOSSICITA'



Proctite attinica



ACUTA: 15-30%



CRONICA: 2-20%

Proctite attinica

Fastidio
Prurito

Tumefazione
Prolasso

Crampi
addominali

Bruciore



Urgency
Incontinenza

Dolore

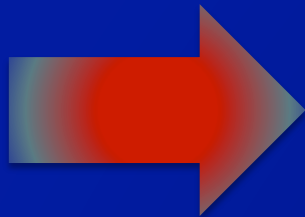
Feci 'mollì'
Diarrea franca

Secrezioni
di muco

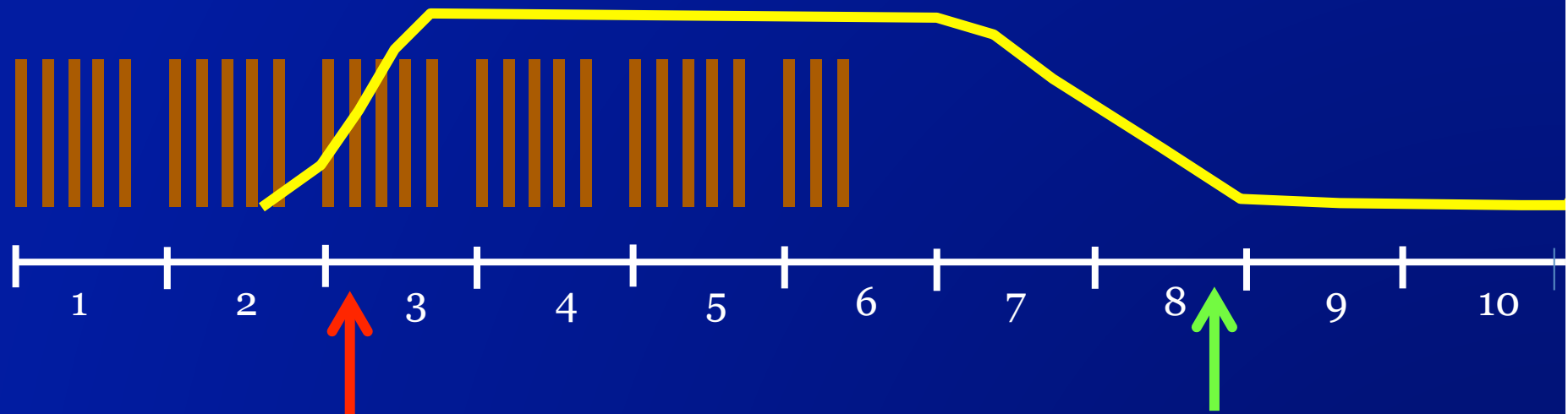
Sanguinamento

Stipsi

Proctite attinica



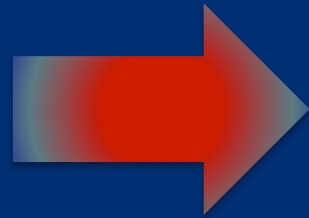
ACUTA



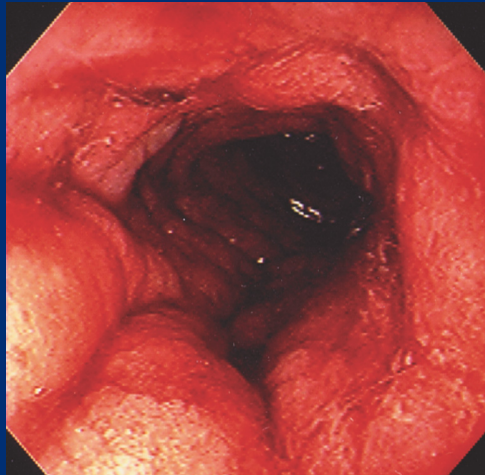
Comparsa: 2-4 settimane da inizio RT

Risoluzione: 1-2 settimane da fine RT

Proctite attinica



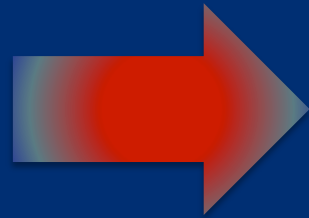
ACUTA



QUADRO ENDOSCOPICO

- ✓ Edema
- ✓ Eritema
- ✓ Friabilità della mucosa
- ✓ Erosioni

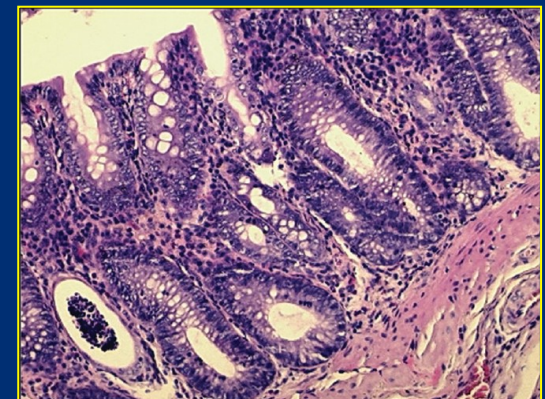
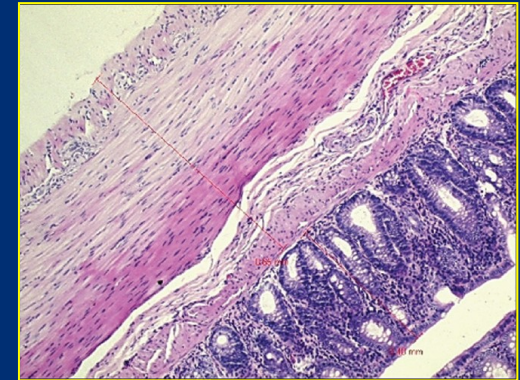
Proctite attinica



ACUTA

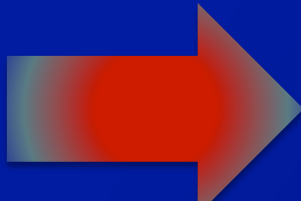
QUADRO ISTOLOGICO

- ✓ Assenza di attività mitotica
- ✓ Perdita o distorsione dell'architettura dei microvilli
- ✓ Infiltrato infiammatorio a carico della mucosa
- ✓ Ascessi criptici
- ✓ Dilatazione di vasi



Courtesy Dott. G. FANELLO

Proctite attinica



ACUTA

Support Care Cancer (2013) 21:313–326
DOI 10.1007/s00520-012-1644-z

SPECIAL ARTICLE

Systematic review of agents for the management of gastrointestinal mucositis in cancer patients

Rachel J. Gibson • Dorothy M. K. Keefe • Rajesh V. Lalla •
Emma Bateman • Nicole Blijlevens • Margot Fijlstra •
Emily E. King • Andrea M. Stringer • Walter J. F. M. van der Velden •
Roger Yazbeck • Sharon Elad • Joanne M. Bowen •
For The Mucositis Study Group of the Multinational
Association of Supportive Care in Cancer/International
Society of Oral Oncology (MASCC/ISOO)

Proctite attinica

Systematic review of agents for the management of gastrointestinal mucositis in cancer patients

- **Revisione sistematica letteratura:** '251 analyzed papers'
- **Tipo terapia oncologica:** RT, CT, HDCT per TMO
- **Obiettivo intervento:** prevenzione, terapia
- **Via di somministrazione:** orale, topica, endovena

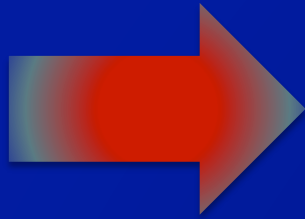
LINEE GUIDA

- **RACCOMANDAZIONE**
- **SUGGERIMENTO**
- **NON POSSIBILE**

Proctite attinica

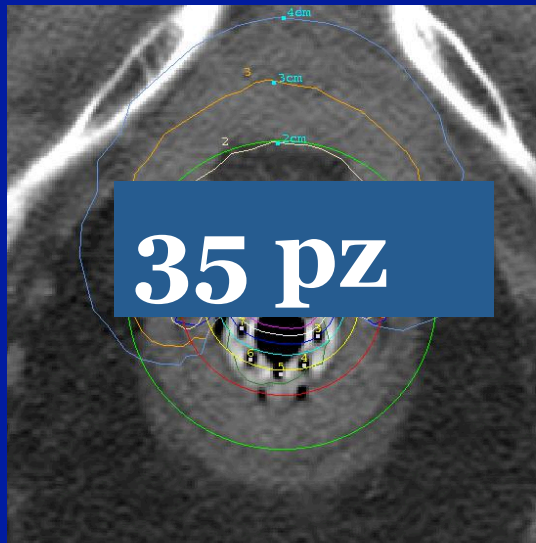
Farmaco	Via somministrazione	Tipo terapia	Linee Guida	Uso
Probiotici lattobacillo	Orale	Prevenzione	Suggestion (3 RCT)	SI
Amifostine	ev	Prevenzione	Recomendation	SI
Sulfasalazina	Orale	Prevenzione	Suggerito	SI
ASA, osalazina, mesalazina	Orale	prevenzione	Recommendation Aumento diarrea	NO
Misoprostolo	Topico	Prevenzione	Recommendation Aumento sanguinamento	NO

Proctite attinica



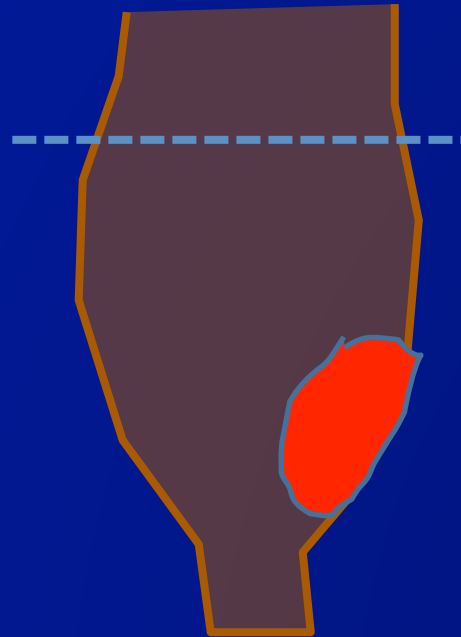
ACUTA: prevenzione

HDR preop RT

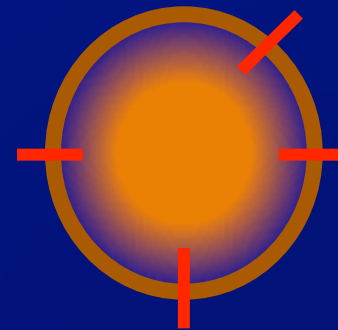


26 Gy 4 frx

Botox injection after last HDR

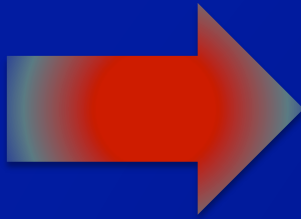


15 pZ
BOTOX



dose escalation: 25 U; 50 U; 100 ; 150 U

Proctite attinica



ACUTA: prevenzione

MTD: 100 U

Anal-pain score 1-10

Table 1. Anal pain score

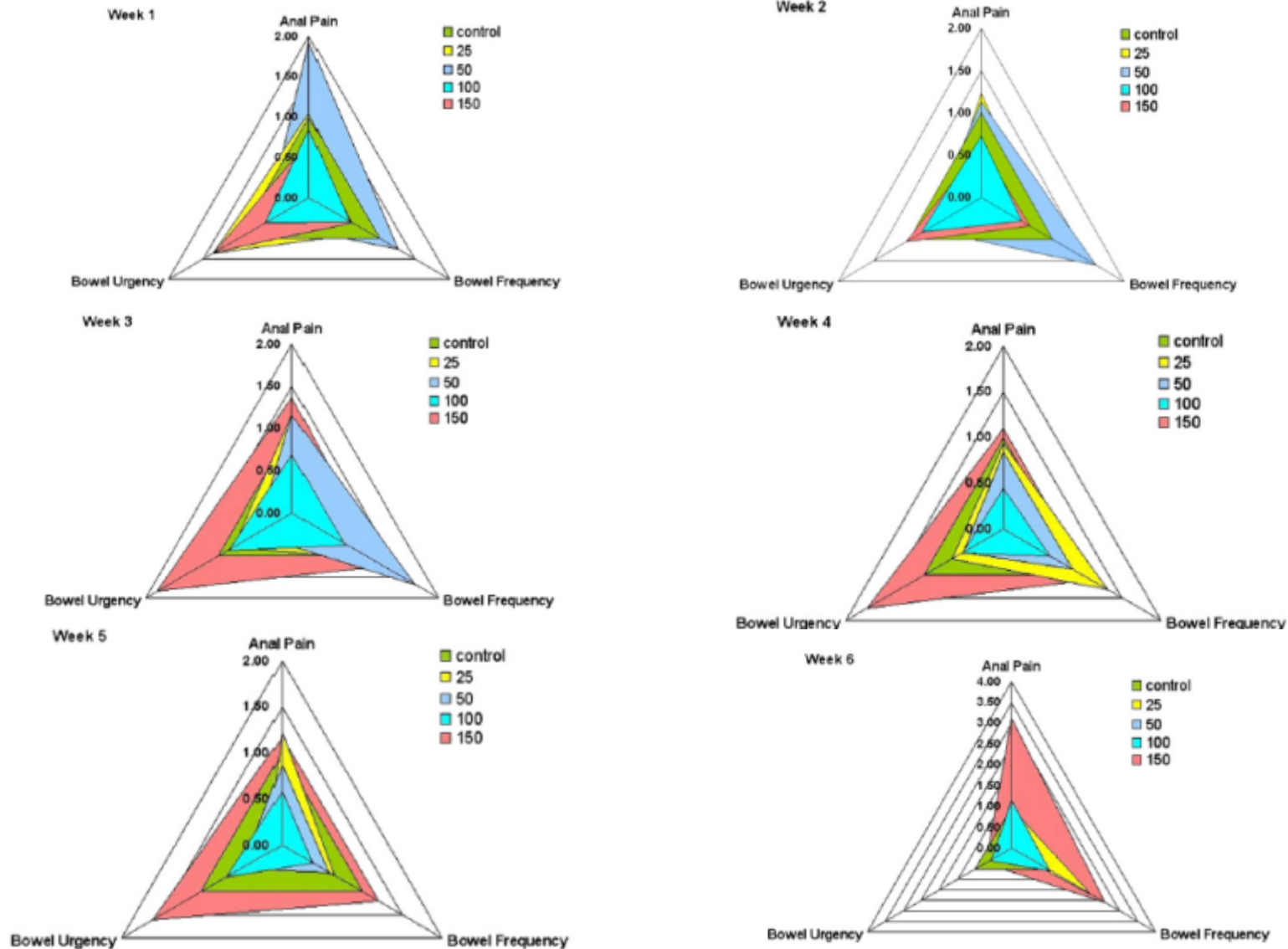
Dose level (U)	Adjusted mean (SE)	Contrast
150	3.94 (0.67)	
100	1.26 (0.54)	<150 U ($p = 0.002$) <50 U ($p = 0.016$) <25 U ($p = 0.014$) <Control ($p = 0.078$)
50	3.35 (0.62)	
25	3.28 (0.62)	
Control	2.88 (0.26)	

Bowel frequency

Table 2. Bowel frequency

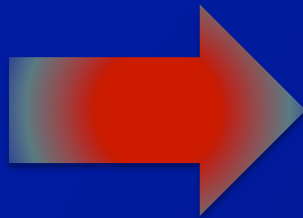
Dose level (U)	Adjusted Mean (STD)	Contrast
150	42.5 (4.7)	> Control ($p = 0.034$)
100	18.3 (3.4)	< 150 U ($p < 0.001$) < 50 U ($p = 0.006$) < 25 U ($p = 0.022$) < Control ($p = 0.016$)
50	34.9 (3.9)	
25	31.9 (3.9)	
Control	29.7 (2.3)	

Proctite attinica



Vuong T et al.
IJROBP 2011

Proctite attinica



CRONICA

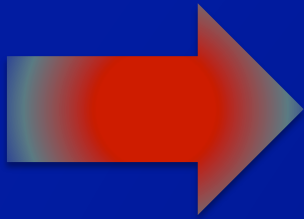
RT



mesi

Comparsa : mesi o anni dalla fine della RT

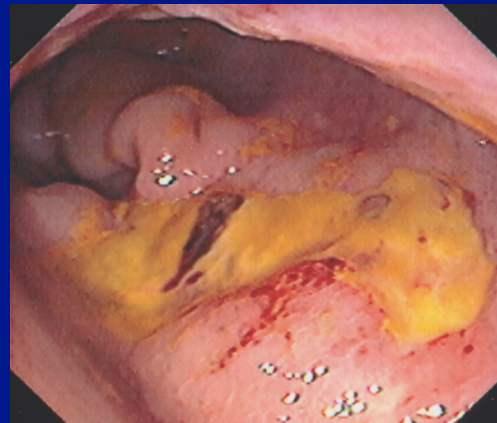
Proctite attinica



CRONICA

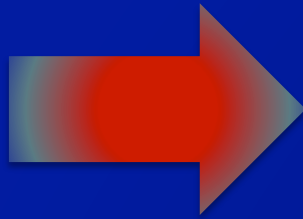
QUADRO ENDOSCOPICO

- ✓ Mucosa friabile e atrofica
- ✓ Teleangectasie
- ✓ Ulcere
- ✓ Fistole (vescica, vagina, intestino)
- ✓ Stenosi
- ✓ Neoplasie "de novo"



Courtesy Dott. G. FANELLO

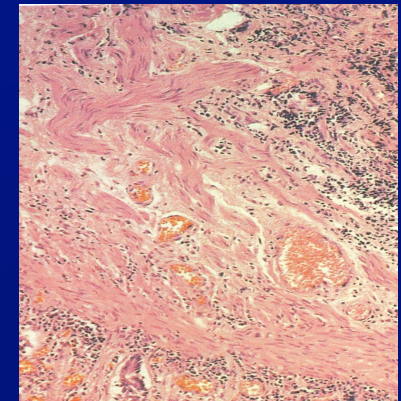
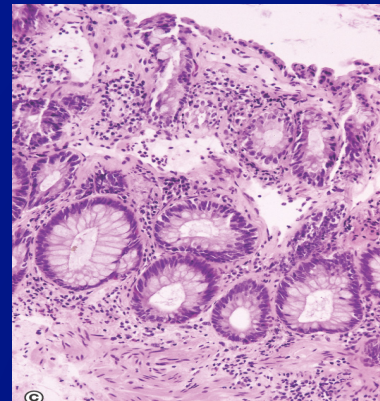
Proctite attinica



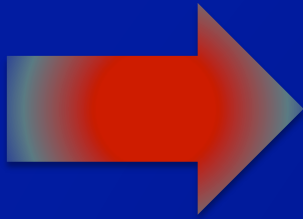
CRONICA

QUADRO ISTOLOGICO

- ✓ Distorsione delle cripte
- ✓ **Fibrosi della sottomucosa**
- ✓ **Endoarterite obliterativa**
- ✓ Neoangiogenesi



Proctite attinica

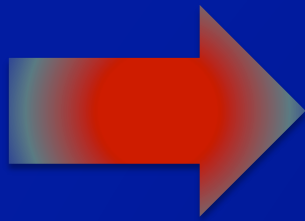


CRONICA

Terapia

- ✓ **Medica**
- ✓ **Topica**
- ✓ **Endoscopica**
- ✓ **Fisica**

Proctite attinica



CRONICA: terapia medica

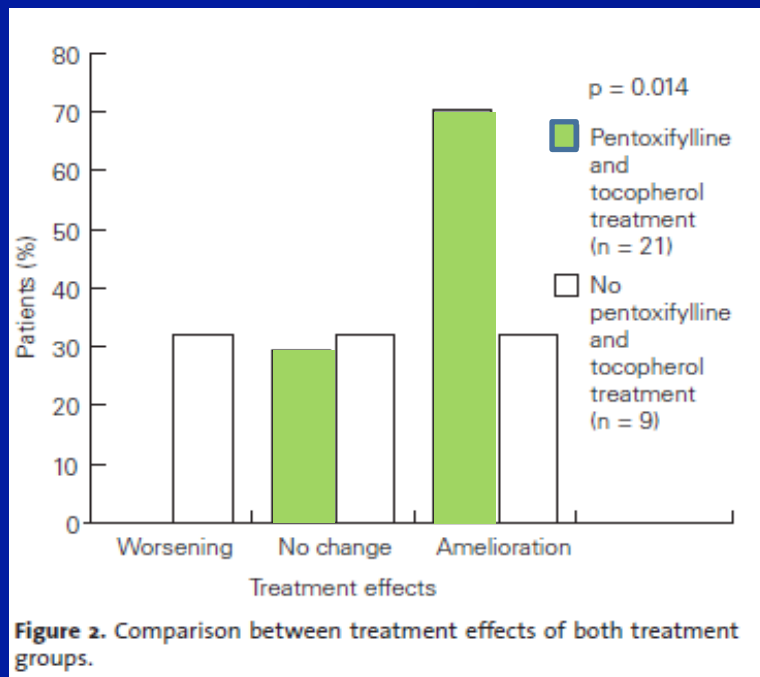
Pentossifillina: 400 mg po 2 vv/die
diminuisce TGF β

Tocoferolo: 500 mg po 2 vv/die
antiossidante

30 pz con proctite cronica:
21 sperimentale; 9 controllo

Proctite attinica

Pentossifillina + Tocoferolo



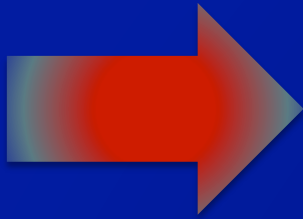
**Median therapy duration:
10 months (6-12)**

**Median time to amelioration:
7 months**

Effetti indesiderati:

ipotensione/cardiovascolari/nausea/aumento di peso

Proctite attinica



CRONICA

Terapia topica

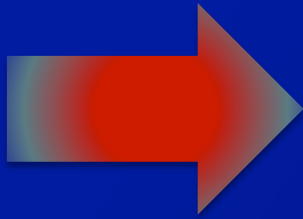
- ✓ Microclismi con sucralfato
- ✓ Microclismi con idrocortisone
- ✓ **Microclismi mesalazina NO**

Sanguinetti G et al. Strahlen Onkol 2003

Fuccio L et al. Alim Pharmacol 2011

Gibson RJ et al. Supp Cancer Care 2013

Proctite attinica

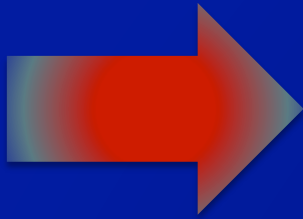


CRONICA

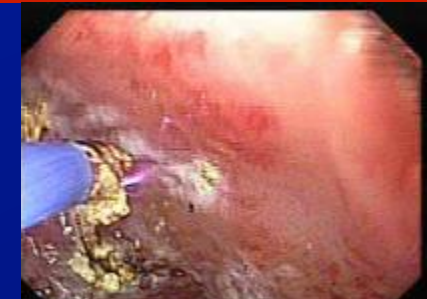
Terapia endoscopica
(sanguinamento refrattario)

- ✓ Argon Plasma Coagulation
- ✓ Crioterapia con Azoto liquido
- ✓ Formalina

Proctite attinica



CRONICA



Argon plasma coagulation

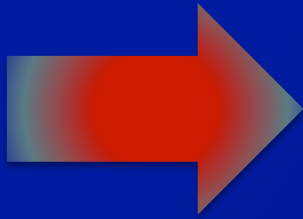
Vantaggi:

- ✓ Successo clinico in 83-95%
- ✓ Ben tollerato
- ✓ Diffuso
- ✓ Costi ridotti

Svantaggi:

- ✓ Ulcere da danno termico
- ✓ Dolore lesioni linea pettinea
- ✓ Non efficaci in sanguinamenti massivi (piccole aree)
- ✓ No protocolli uniformi

Proctite attinica



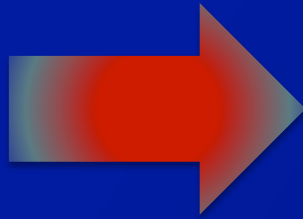
CRONICA

Terapia fisica

**Ossigeno
iperbarico
(HBO)**



Proctite attinica



CRONICA

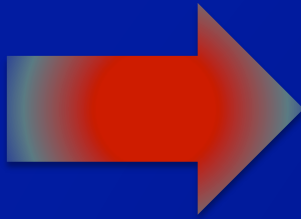
HBO

Stimola

- ✓ Angiogenesi (VEGF)
- ✓ Proliferazione osteoblasti
- ✓ Proliferazione fibroblasti
- ✓ Formazione di collagene

Aumento intracellulare di O₂

Proctite attinica



CRONICA: HBO

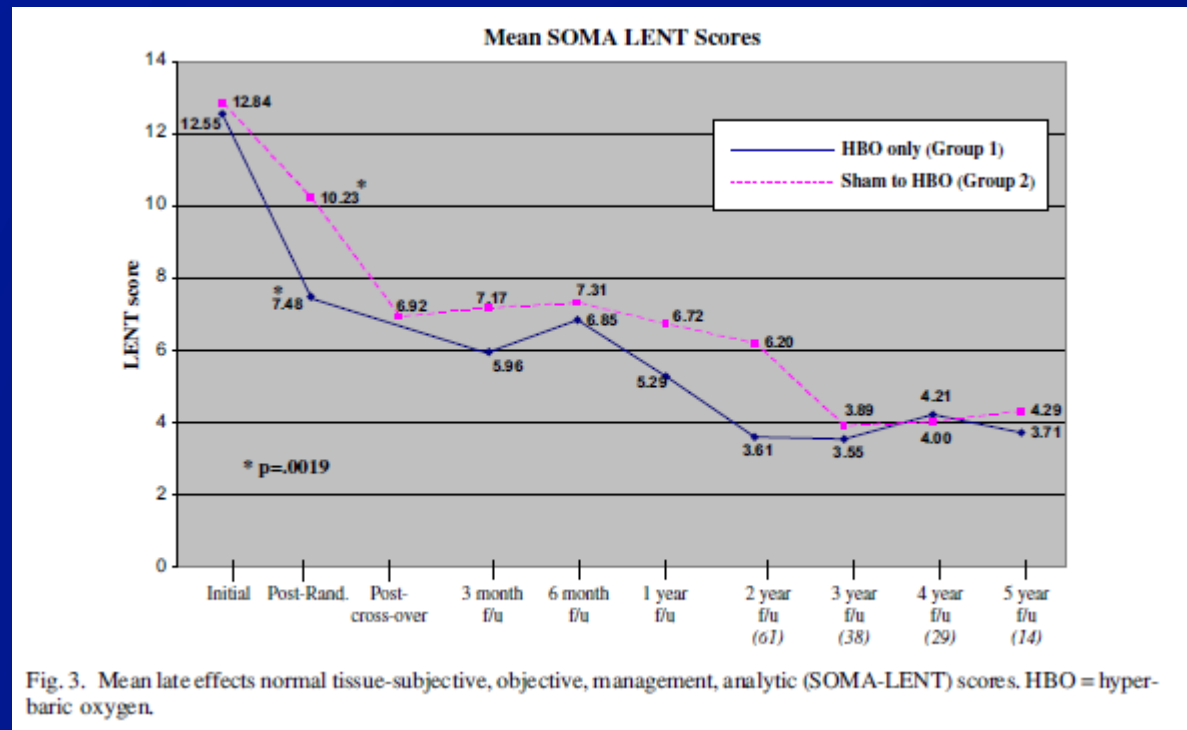
120 pazienti valutabili

Studio
randomizzato,
in doppio
cieco,
multicentrico

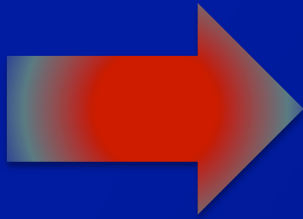
Valutazione

SOMA LENT, Questionari

QoL , tempo



Proctite attinica



CRONICA: HBO

Riposta: 85%, CR: 36%

Tossicità:

- ✓ Ansia
- ✓ Barotrauma orecchio (15%)
- ✓ Barotrauma sinusale
- ✓ Miopia temporanea

Controindicazioni:

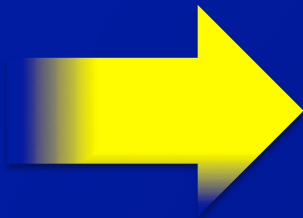
- ✓ Pregressi pnx
- ✓ Enfisema
- ✓ Crisi epilettiche non trattate
- ✓ Insufficienza cardiaca

NON stimola crescita TUMORALE!!

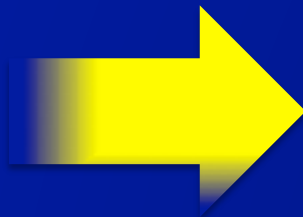
F L O W - C H A R T

Grado	Terapia	Sintomi persistenti
Grado 1-2 Urgenza occasionale intermittente, sangue occulto, sanguinamento occasionale, stenosi lieve moderata, ulcere superficiali o < 1cm	Antinfiammatori os (mesalazina , corticosteroidi), Antiossidanti os	Sucralfato topico
Grado 3 Urgenza , dolore, sanguinamento persistenti; stenosi grave, ulcera profonda	Antinfiammatori, antiossidanti, sucralfato, HBO	Argon Plasma, Formalina
Grado 4 Urgenza grave, dolore incotrollabile, grave sanguinamento, perforazione fistola ostruzione completa	Chirurgia	

Cistite attinica



ACUTA: 25-30%



CRONICA: 20%
(9% ematuria macro ricorrente)

Cistite attinica

Disuria

Urgency

Pollachiuria

Bruciore

Incontinenza

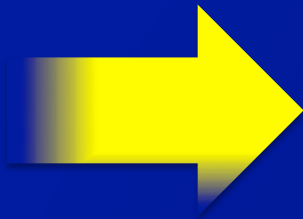
Dolore

Ostruzione

Sanguinamento



Cistite attinica

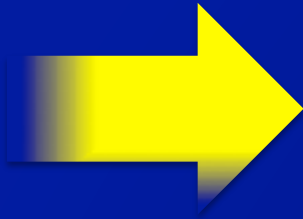


ACUTA

Terapia sintomatica

- ✓ **Anticholinergic drugs**
- ✓ Phenazopyridine hydrochloride
- ✓ Flavoxate hydrochloride
- ✓ **alpha1-adrenoreceptor blockade**

Cistite attinica



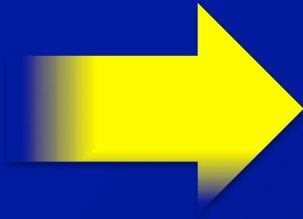
ACUTA: prevenzione

Crumberry

Prohantocyanina

- ✓ Azione anti-adesione E.Coli
- ✓ Beneficio clinico: ore
- ✓ Dose 300 mg/die
- ✓ Durata: 10 h
- ✓ 2 bicchieri succo

Cistite attinica



**ACUTA: prevenzione
crumberry**

RCT doppio cieco

**Gruppo 1:
Crumberry ***

**Gruppo 2:
PLACEBO**

*juice twice a day

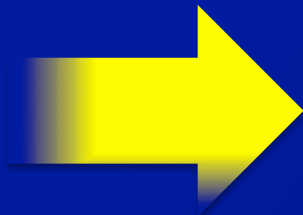
6 settimane

Valutazione

Diario sintomi, campioni urine

Cowan CC et al. Clinical Oncol 2012

Cistite attinica



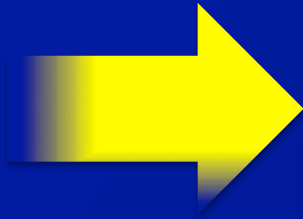
ACUTA: Crumberry 128 pz

Patients in the compliant population who experienced an increase in urinary symptoms or deterioration of the worst grade of urinary symptoms experienced during treatment and follow-up

Increased urinary symptoms or Worst grade of urinary symptoms experienced during treatment and follow-up	Arm				Compliant population			
	Intention-to-treat		Per-protocol		Cranberry		Placebo	
	Count	%	Count	%	Count	%	Count	%
0	2	3.5%	6	10.5%	0	0.0%	1	7.1%
1	21	54.4%	20	35.1%	13	72.2%	7	50.0%
2	17	29.8%	17	29.8%	3	16.7%	3	21.4%
3	7	12.3%	14	24.6%	2	11.1%	3	21.4%
Total	57*	100.0%	57*	100.0%	18	100.0%	14	100.0%

Not significant!

Cistite attinica



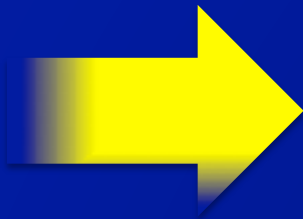
ACUTA: **crumberry**

RCT 150 pz

Tossicità G2-G3	
Cistiflux	13,3% (10/75)
Controllo	22,6% (17/75)

Tossicità G2-G3	Settimane di RT							
	1	2	3	4	5	6	7	8
Cistiflux	0% (0/75)	1,3% (1/75)	4,0% (3/75)	8,0% (6/75)	8,0% (6/75)	8,0% (6/75)	13,2% (9/68)	25% (1/4)
Gruppo controllo	0% (0/75)	0% (0/75)	2,7% (2/75)	5,3% (4/75)	8% (6/75)	16% (12/75)	23,85 (15/63)	40% (2/5)

Cistite attinica



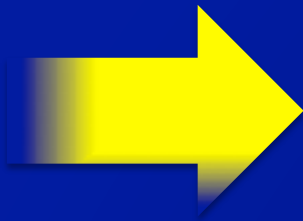
CRONICA

RT



Comparsa : mesi o anni dalla fine della RT

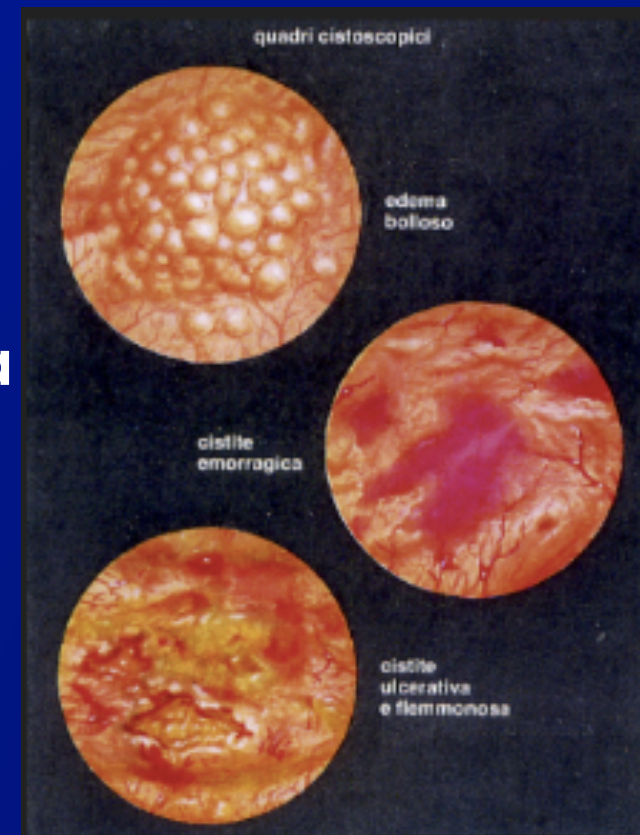
Cistite attinica



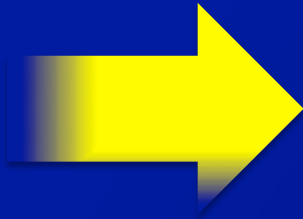
CRONICA

QUADRO CISTOSCOPICO

- ✓ Edema
- ✓ Eritema
- ✓ Telenagectasia
- ✓ Ulcere Sanguinanti
- ✓ Fistole
- ✓ Fibrosi
- ✓ Ridotta capacità



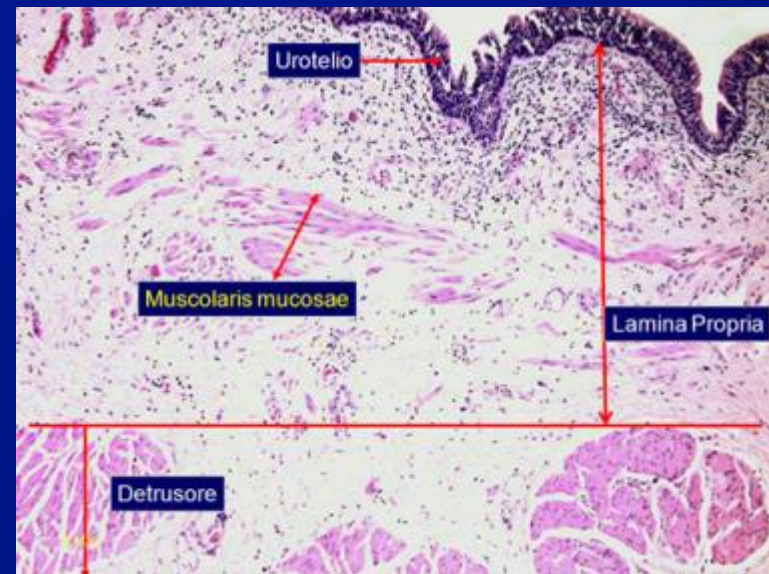
Cistite attinica



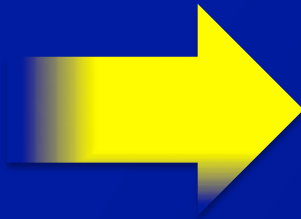
CRONICA

QUADRO istologico

- ✓ Alterazioni **vascolari** (iperplasia, occlusione, fibrosi)
- ✓ Alterazioni muscolari
- ✓ Ischemia
- ✓ **Fibrosi**



Cistite attinica



CRONICA

Practical treatment approach of radiation induced cystitis

R. Martínez-Rodríguez*, J. Areal Calama, O. Buisan Rueda, C. González Satue,
J. Sanchez Macias, M. Arzoz Fabregas, J. Gago Ramos, S. Bayona Arenas, L. Ibarz Servio,
and J.M. Saladié Roig

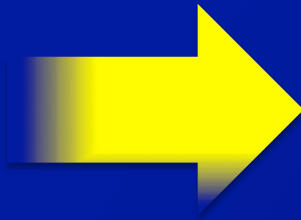
Urology Service, Hospital Germans Trias i Pujol, Badalona, Spain

Systemic

Intravesical

Physical

Cistite attinica



CRONICA

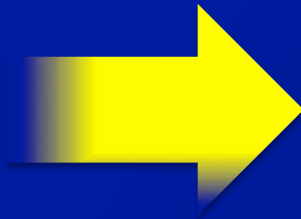
Practical treatment approach of radiation induced cystitis

Sistemica

- ✓ *Estrogeni coniugati* *citochine* *Ipercoagulabilità*
- ✓ *Sodio polisolfato* *GAG* *laboratorio* *Rapida azione /sicuro*
- ✓ *Acido aminocaproico* *trattamenti brevi*
- ✓ *Fattore VIIa ricombinante* *Uso compassionevole*

Livello Evidenza IV

Cistite attinica



CRONICA

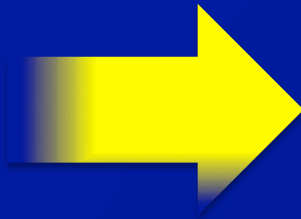
Practical treatment approach of radiation induced cystitis

Intravesiciale

- ✓ *Acido ialuronico* *Riparazione* *Effetti collaterali*
- ✓ *Alluminio* *riparazione* *capillari* *Effetti collaterali locali e sistemici* (*lesioni ampie*)
- ✓ *Formalina* *Efficacia* *Effetti collaterali locali e sistemici*

Livello Evidenza III

Cistite attinica



CRONICA

Fisica

✓ *Internal iliac artery embolization*

Dolore gluteo/paralisi/necrosi

✓ *Helmstein b... estension* *Durata 6 mesi*

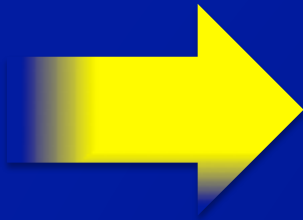
Rottura ve...

✓ *HyperBaric Oxigen*

✓ *Cystectomy*

Livello Evidenza IV

Cistite attinica



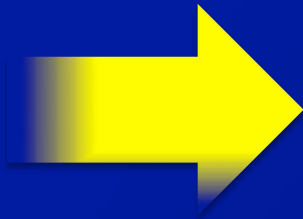
CRONICA

Practical treatment approach of radiation induced cystitis

LIEVE

Initiate ambulatory hyaluronic acid instillations
Program hyperbaric chamber

Cistite attinica



CRONICA

Practical treatment approach of radiation induced cystitis

Anemia

Urethrocytography in the operating room: evacuation of clots, electrocauterization of suspicious areas, and biopsies.

Program hyperbaric chamber ←

Oral treatment: ←

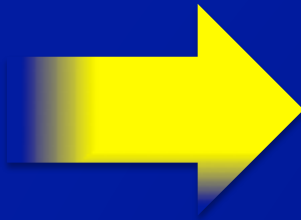
Pentosan polysulfate

Conjugated estrogens

Aminocaproic acid

Intravesical instillations: aluminum salts. ←

Cistite attinica



CRONICA

Practical treatment approach of radiation induced cystitis

**Emorragia
non
controllabile**



Embolization



Helmstein balloon



Formalin instillation



Cystectomy

Terapia di supporto: pelvi

- ✓ **Consolidata pratica clinica**
- ✓ **Numerosi studi**
- ✓ **Evidenze deboli**
- ✓ **Misurazione tossicità**
- ✓ **Protocolli, GL**
- ✓ **Gestione in MDT casi complicati**

