Associazione Italiana
Radioterapia Oncologica
Gruppo Interregionale
Lazio/Abruzzo/Molise

# Le terapie di supporto in Radioterapia:

## Verso una Guida Pratica

Lunedì 4 Dicembre 2017
Centro Studi Cardello
Via del Cardello 24 – Roma

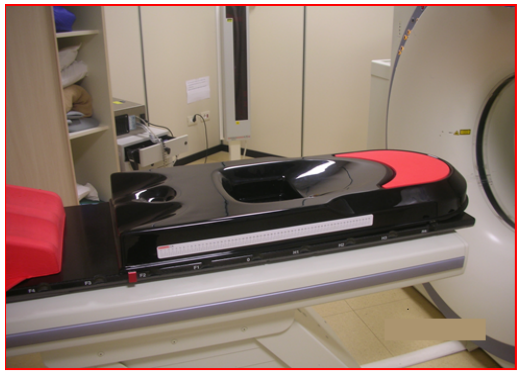
# Enterocolite

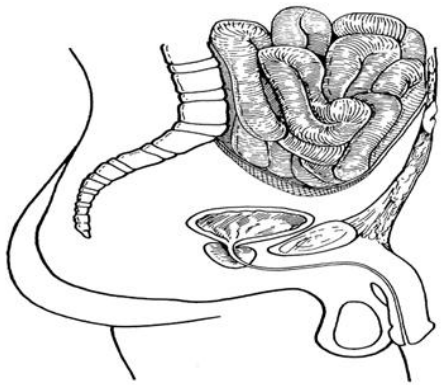
## Presidi di prevenzione e trattamento

*Carlo Greco*

UNIVERSITA' CAMPUS BIO-MEDICO DI ROMA

Università Campus Bio-Medico di Roma - Via Álvaro del Portillo, 21 - 00128 Roma – Italia
www.unicampus.it

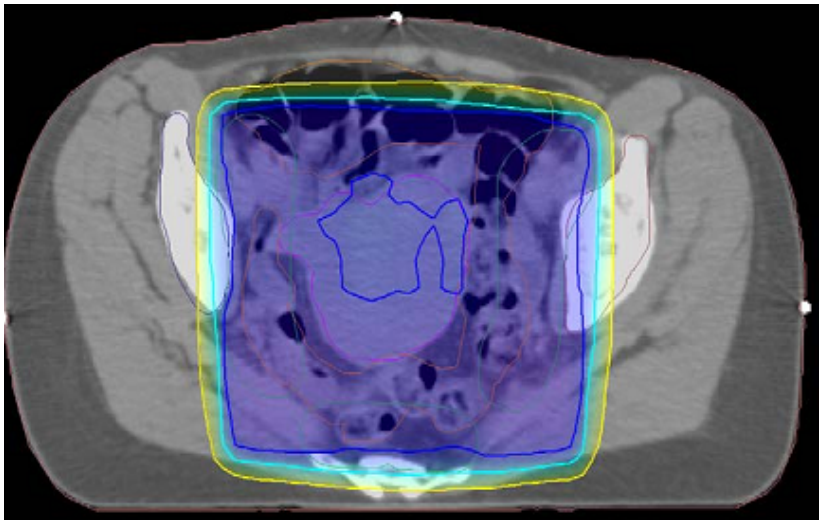




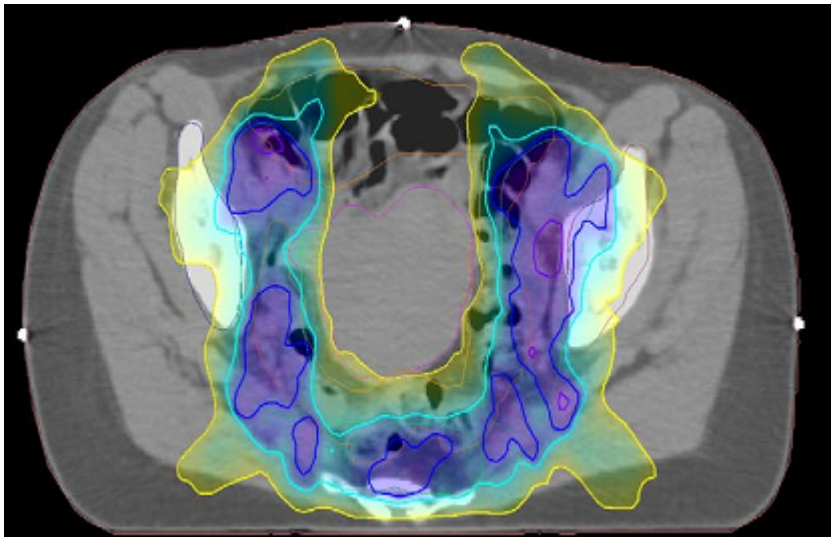
- **presidi per dislocare il tenue**
- **posizionamento chirurgico** di "Absorbable mesh sling"

**Adli M.** et al.Int.J Radiat.Oncol.Biol.Phys 2003
**Allial AS**. et al. Strahlenther.Onkol 2002
**Ahmad R.** et al.Radiother.Oncol 2008
**Tuech JJ .**et al.Eur J Surg Oncol 2004

# OTTIMIZZAZIONE DELLE TECNICHE DI TRATTAMENTO



3DCRT



IMRT

# DOSE CONSTRAINTS

ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. 76, No. 3, Supplement, pp. S10–S19, 2010

0360-3016/10/$–see front matter

doi:10.1016/j.ijrobp.2009.07.1754

**INTRODUCTORY PAPER**

## USE OF NORMAL TISSUE COMPLICATION PROBABILITY MODELS IN THE CLINIC

LAWRENCE B. MARKS, M.D.,* ELLEN D. YORKE, PH.D.,† ANDREW JACKSON, PH.D.,†
RANDALL K. TEN HAKEN, PH.D.,‡ LOUIS S. CONSTINE, M.D.,§ AVRAHAM EISBRUCH, M.D.,‡
SØREN M. BENTZEN, PH.D.,‖ JIHO NAM, M.D.,* AND JOSEPH O. DEASY, PH.D.¶

| Organ | Volume segmented | Irradiation type (partial organ unless otherwise stated)† | Endpoint | Dose (Gy), or dose/volume parameters† | Rate (%) | Notes on dose/volume parameters |
|---|---|---|---|---|---|---|
| Small bowel | Individual small bowel loops | 3D-CRT | Grade ≥ 3 acute toxicity§ | V15 <120 cc | <10 | Volume based on segmentation of the individual loops of bowel, not the entire potential peritoneal space |
| | Entire potential space within peritoneal cavity | 3D-CRT | Grade ≥ 3 acute toxicity§ | V45 <195 cc | <10 | Volume based on the entire potential space within the peritoneal cavity |

Forza della raccomandazione positiva debole (Grado B)

# PREVENZIONE





# ALIMENTAZIONE

Ridotto introito di **fibre insolubili** e **lattosio** può ridurre la tossicità gastrointestinale

Liu L et al., Int JRadiatOncolBiol-Phys 1997;38:65–71

Wedlake L, et al., Eur J Cancer 2008;44:2212–7.

# Nutritional interventions for reducing gastrointestinal toxicity in adults undergoing radical pelvic radiotherapy (Review)

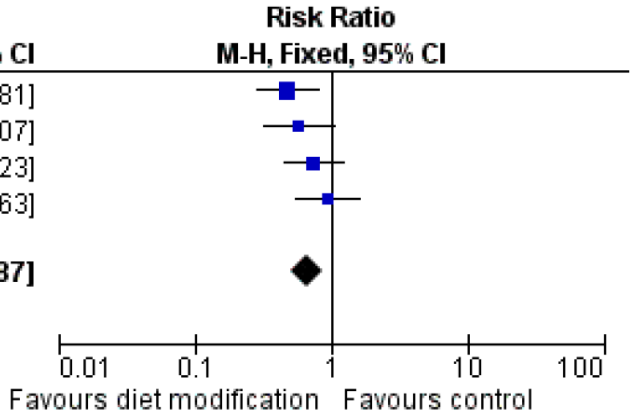
Henson CC, Burden S, Davidson SE, Lal S

Cochrane Library
Cochrane Database of Systematic Reviews

**Forest plot of comparison: 1 Nutritional intervention versus no nutritional intervention, outcome: 1.1 Diarrhoea.**

| Study or Subgroup | Nutritional intervention Events | Total | Control Events | Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Bye 1992 | 14 | 61 | 32 | 67 | 34.6% | 0.48 [0.28, 0.81] |
| Murphy 2000 | 10 | 30 | 17 | 30 | 19.3% | 0.59 [0.32, 1.07] |
| Pettersson 2012 | 18 | 61 | 23 | 58 | 26.7% | 0.74 [0.45, 1.23] |
| Wedlake 2012 | 24 | 70 | 13 | 36 | 19.5% | 0.95 [0.55, 1.63] |
| **Total (95% CI)** | | **222** | | **191** | **100.0%** | **0.66 [0.51, 0.87]** |
| Total events | 66 | | 85 | | | |

Heterogeneity: Chi² = 3.50, df = 3 (P = 0.32); I² = 14%
Test for overall effect: Z = 3.01 (P = 0.003)




Risk of diarrhoea was 44% in the control group and 30% in the intervention group. The relative effect was 0.66 (95% CI 0.51 to 0.87) for dietary modification

# NUTRIZIONE ELEMENTARE

Le formule nutrizionali elementali forniscono macro e micro nutrienti essenziali (aminoacidi, grassi, carboidrati, vitamine, minerali) in una forma liquida e predigerita facilmente assimilabili.
Possono essere somministrati in flaconcini o tramite sondino naso-gastrico ed essere utilizzate come unica fonte di nutrimento per periodi di tempo prolungati.

# Clinical trial: normal diet vs. partial replacement with oral E028 formula for the prevention of gastrointestinal toxicity in cancer patients undergoing pelvic radiotherapy

C. MCGOUGH*, L. WEDLAKE*, C. BALDWIN†, C. HACKETT†, A. R. NORMAN‡, P. BLAKES,

Table 2. Summary of patient characteristics

| | Group 1 (intervention) | Group 2 (no intervention) |
|---|---|---|
| *n* | 25 | 25 |
| Age (median and range) | 62.5 (29–79) | 58 (38–82) |
| Gender (F:M) | 17:8 | 12:13 |
| Radiotherapy dose (Gy) | 50.4 (45–70) | 54 (45–70) |
| Site | | |
| Endometrium | 8 | 5 |
| Cervix | 5 | 2 |
| Ovary | 0 | 1 |
| Bladder | 1 | 1 |
| Prostate | 3 | 8 |
| Rectum | 5 | 4 |
| Anus | 3 | 1 |
| Other | 0 | 3 |
| Concomitant chemotherapy | 11 (44%) | 7 (28%) |
| Weight (kg) | 80 (57.2–105.8) | 82.5 (59.9–124.1) |
| BMI (kg/m$^2$) | 29 (22–39) | 29 (22–41) |

patients in the intervention group were asked to replace one meal per day, equivalent to 33% of total caloric requirements, with elemental diet.

**Patients taking elemental diet did not have lower gastrointestinal toxicity ratings or inflammatory markers (P > 0.2).**




Alimen t Pharma col Ther 27 , 1132–113 9 2008

# Consigli alimentari nella prevenzione dell'enterite attinica

| | Cibi permessi | Cibi da evitare |
|---|---|---|
| Cereali | Riso, pasta, semolino, pane bianco | Alimenti preparati con farine integrali |
| Verdure | Carote, patate, zucchine, preferibilmente bollite | Tutto il resto |
| Frutta | Mele, banane | Tutto il resto, compresa la frutta secca |
| Latte e formaggi | Parmigiano, grana | Tutto il resto |
| Carni | Carni bianche o rosse magre, ai ferri, al vapore e bollite, prosciutto cotto o crudo, bresaola | Maiale, insaccati, salumi, carni affumicate, selvaggina, carni fritte |
| Pesce | Pesce magro | Pesce grasso e pesce fritto |
| Condimenti | Olio extravergine di oliva | Burro, maionese, salse piccanti |
| Dolci | Biscotti secchi non integrali e poveri di grassi | Crema, panna, cacao, gelati alla crema e alla frutta, dolci in genere |
| Bevande | Acqua, camomilla, thè, caffè d'orzo, yogurt bianco e magro | Gassate, fredde, caffè, latte, alcolici |
| Uova | Uova lesse | Uova fritte o a frittata |

**Raccomandazione positiva debole (Grado B)**

# INTEGRATORI E ANTINFIAMMATORI



www.impactjournals.com/oncotarget/ Oncotarget, 2017, Vol. 8, (No. 18), pp: 30595-30605

Review

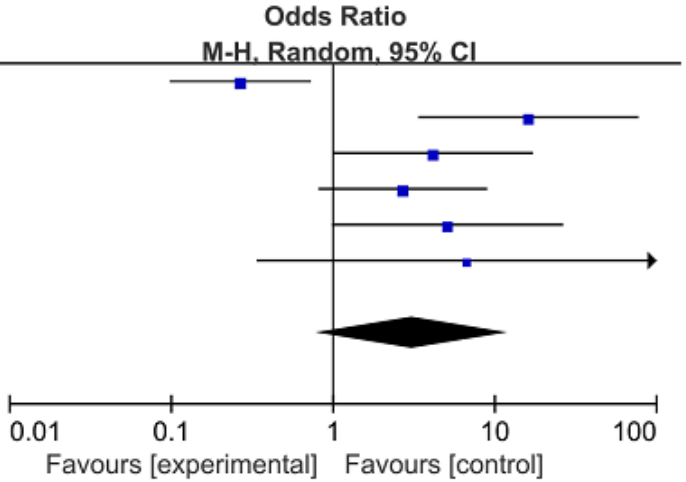
# Therapeutic role of glutamine in management of radiation enteritis: a meta-analysis of 13 randomized controlled trials

De-dong Cao[1], Hui-lin Xu[2], Min Xu[1], Xiang-yun Qian[1], Zhu-cheng Yin[1] and Wei Ge[1]

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Odds Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Qi, 2011 | 8 | 38 | 19 | 38 | 19.5% | 0.27 [0.10, 0.73] |
| Rao, 2009 | 43 | 45 | 20 | 35 | 16.9% | 16.13 [3.36, 77.34] |
| Wu, 2011 | 29 | 32 | 21 | 30 | 17.7% | 4.14 [1.00, 17.18] |
| Yang, 2004 | 31 | 36 | 23 | 33 | 18.7% | 2.70 [0.81, 8.96] |
| Zhang, 2012 | 28 | 30 | 22 | 30 | 16.6% | 5.09 [0.98, 26.43] |
| Zhou, 2007 | 8 | 8 | 16 | 22 | 10.6% | 6.70 [0.34, 133.59] |
| **Total (95% CI)** | | **189** | | **188** | **100.0%** | **3.07 [0.79, 11.96]** |
| Total events | 147 | | 121 | | | |

Heterogeneity: Tau² = 2.20; Chi² = 25.36, df = 5 (P = 0.0001); I² = 80%

Test for overall effect: Z = 1.61 (P = 0.11)




**The results of meta-analysis showed that the total efficy of glutamine was higher for patients with radiation enteritis compared with that in control group, however, there was no statistically signifiant diffrence (OR = 3.07, 95%CI: 0.79-11.96; *P* > 0.05)**

# Studies on prevention of radiation enteritis with 5-aminosalicylates

| author | type of study | number of patients | therapy | result |
|---|---|---|---|---|
| Kilic et al. 2000 | double-blind, randomised, placebo-controlled | 87 during pelvic radiation with 46 – 50 Gy | 2 g sulfasalazine vs. placebo over 5 weeks | less diarrhoea (55 vs. 86 %, p = 0.001) and less severe diarrhoea (p = 0.038) in sulfasalzine group |
| Resbeut et al. 1997 | double-blind, randomised, placebo-controlled, multicenter | 153 during pelvic radiation with 45 – 50 Gy | 4 g mesalazine vs. placebo over 80 days | no difference |
| Baughan et al. 1993 | double-blind, randomised, placebo-controlled | 73 during pelvic radiation with 30 – 60 Gy | 5-ASA 800 mg vs. placebo until 4 weeks after radiation | more diarrhoea (92 vs. 74 %, p = 0.07), more severe and frequent diarrhoea (p = 0.014 / 0,026) in 5-ASA group |
| Martenson et al. 1996 | double-blind, randomised, placebo-controlled | 58 during pelvic radiation; 6 with concomitant 5-Fu (3 in each group) | Olsalazine 2 × 500 mg/d vs. placebo | more diarrhoea and more severe diarrhoea in olsalazine group (p = 0.0036), study prematurely terminated |

Zimmerer T et al.,Z Gastroenterol 2008; 46: 441–448

# Studies on prevention of radiation enteritis with sucralfate

| author | type of study | number of patients | therapy | result |
|---|---|---|---|---|
| Henriksson et al. 1992 | double-blind, placebo-controlled | 70 during pelvic radiation with 64 Gy | sucralfate 6 g/d, 2 weeks after beginning of radiation therapy over 6 weeks | significantly less stool frequency in sucralfate group |
| Martenson et al. 2000 | double-blind, randomised, placebo-controlled | 123 during pelvic radiation with 45 – 53 Gy; 11 with concomitant 5-FU | sucralfate 1.5 g every 6 h vs. placebo | more frequent incontinence (34 vs. 16 %, p = 0.04), more frequent nausea (p = 0.03) in sucralfate group |
| Stellamans et al. 2002 | double-blind, randomised, placebo-controlled | 80 during pelvic radiation with 45 – 66 Gy; 40 with concomitant chemotherapy (19/21) | sucralfate 4 g in 4 doses until finish of radiation therapy vs. placebo | no difference between sucralfate or placebo group |
| Valls et al. 1999 | double-blind, randomised, placebo-controlled | 120 during pelvic radiation with 45 – 50 Gy | sucralfate 2 g three times a day | no difference in stool frequency, less diarrhoeal stools and use of loperamide in the sucralfate group |

Zimmerer T et al.,Z Gastroenterol 2008; 46: 441–448

RESEARCH ARTICLE

# Probiotics for prevention of radiation-induced diarrhea: A meta-analysis of randomized controlled trials

Meng-Meng Liu, Shu-Ting Li, Yan Shu, He-Qin Zhan*

| Study or Subgroup | Probiotics Events | Probiotics Total | Control Events | Control Total | Weight | Risk Ratio IV, Random, 95% CI |
|---|---|---|---|---|---|---|
| Castro 2009 | 7 | 20 | 13 | 20 | 15.5% | 0.54 [0.27, 1.06] |
| Chitapanarux 2010 | 3 | 32 | 14 | 31 | 9.8% | 0.21 [0.07, 0.65] |
| Delia 2007 | 42 | 243 | 119 | 239 | 20.8% | 0.35 [0.26, 0.47] |
| Demers 2014 | 90 | 140 | 68 | 86 | 22.2% | 0.81 [0.69, 0.96] |
| Giralt 2008 | 30 | 44 | 24 | 41 | 20.5% | 1.16 [0.84, 1.62] |
| Salminen 1988 | 3 | 11 | 8 | 10 | 11.2% | 0.34 [0.12, 0.94] |
| **Total (95% CI)** | | **490** | | **427** | **100.0%** | **0.55 [0.34, 0.88]** |
| Total events | 175 | | 246 | | | |

Heterogeneity: $Tau^2 = 0.26$; $Chi^2 = 39.88$, $df = 5$ ($P < 0.00001$); $I^2 = 87\%$

Test for overall effect: $Z = 2.50$ ($P = 0.01$)

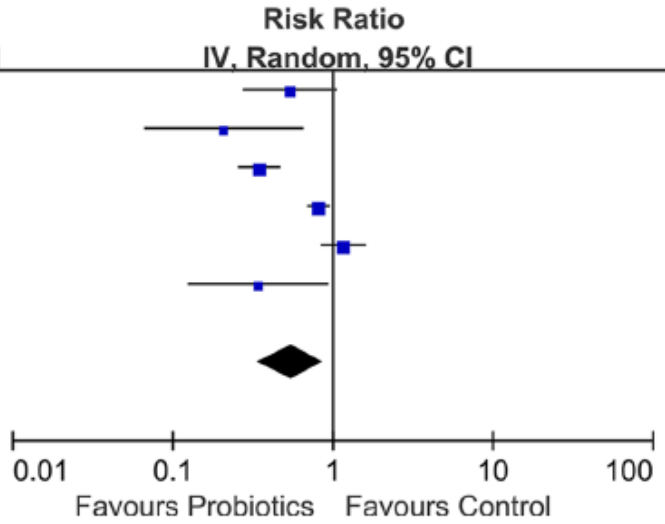



**Fig 4. Effect of probiotics on prevention of radiation-induced diarrhea compared with placebo.**

Probiotics may be beneficial to prevent radiation-induced diarrhea in patients who suffered from abdominal or pelvic cancers during radiotherapy period

Plos one June 2, 2017

I Probiotici sono facili da usare e non generano effetti avversi e possono essere utilizzati per la profilassi di diarrea indotta da radiazioni.

[Forza della raccomandazione positiva debole (Grado B)]



Sucralfato, Aminosalicilati e Glutamina non dovrebbero essere somministrati [Forza della raccomandazione negativa forte (Grado B)]

# TERAPIA

**Idratazione**
**Probiotici**
**Loperamide**
**Octreotide**

# Probiotici

**Results of a double-blind, randomized study to evaluate the efficacy and safety of Antibiophilus in patients with radiation-induced diarrhoea.**


206 recruited patients

Antibiophilus patients showed superiority with respect to the number of bowel movements ($P < 0.10$) and faeces consistency ratings by the investigators ($P < 0.05$) at the study end

Urbancsek H et al.,European Journal of Gastroenterology & Hepatology. 13(4):391-396, APR 2001

# Loperamide

**Studies using loperamide in patients with diarrhea following telecobalt irradiation of malignant abdominal tumors**

45 patients suffering from radiation-induced diarrhoea with loperamide at 2 – 4mg per day and achieved normalisation of the frequency of bowel movements in 42 out of 45 patients after a mean of 6.4 days



Geginat et al., Strahlentherapie 1978; 154: 11–15

# Octreotide

The somatostatin analogue octreotide has been shown to be effective against chemotherapy-induced diarrhea

Zidan Jet al. Octreotide in the treatment of severe chemotherapy- induced diarrhea. Ann Oncol 2001; 12: 227–229

Wang and colleagues reported that octreotide reduced the transmigration of granulocytes and intestinal wall thickening in radiation exposed bowels of rats

Wang J, Zheng H, Sung CC et alInt J Radiat Oncol Biol Phys 1999; 45: 1289–1296

# THE EFFICACY OF OCTREOTIDE IN THE THERAPY OF ACUTE RADIATION-INDUCED DIARRHEA: A RANDOMIZED CONTROLLED STUDY

MELEK N. YAVUZ, M.D.,* A. AYDIN YAVUZ, M.D.,* FAZIL AYDIN, M.D.,† GAMZE CAN, M.D.,‡ AND HALIL KAVGACI, M.D.†

**61 patients with Grade 2 (four to six stools per day) or Grade 3 ( > seven stools per day, NCI Common Toxicity Criteria) diarrhea associated with pelvic radiotherapy were assigned randomly to receive octreotide s.c., 100 g three times daily (n=33) or diphenoxylate and atropine orally, 2.5 mg four times daily (*n*=28).**

The standardized irradiation protocol consisted of wholepelvis external irradiation >45 Gy in >4.5 weeks with a daily dose 1.8 –2.0 Gy

All patients were treated in supine position without any bowel immobilization devices, with LINAC or 60Co teleteraphy machines.
All patients received a low fiber and low lactose diet during radiation treatment.

Int. J. Radiation Oncology Biol. Phys., Vol. 54, No. 1, pp. 195–202, 2002

| Outcome | Number of patients: Octreotide ($n$ = 33) | Number of patients: Diphenoxylate ($n$ = 28) | |
|---|---|---|---|
| Duration of diarrhea (days) | 3.30 ± 0.3 | 5.36 ± 0.4 | $t = -4.21$, $p = 0.0001$ |
| (range) | (1–7) | (2–11) | |
| Success* | 20 (61%) | 4 (14%) | $x^2 = 11.8$, $p = 0.002$ |
| Failure† | 1 (3%) | 3 (7%) | $p = 0.33$‡ |
| Duration of radiotherapy interruption (days) | 0.45 ± 0.2 | 1.89 ± 0.5 | $z = 2.99$, $p = 0.003$§ |
| (range) | (0–4) | (0–8) | |

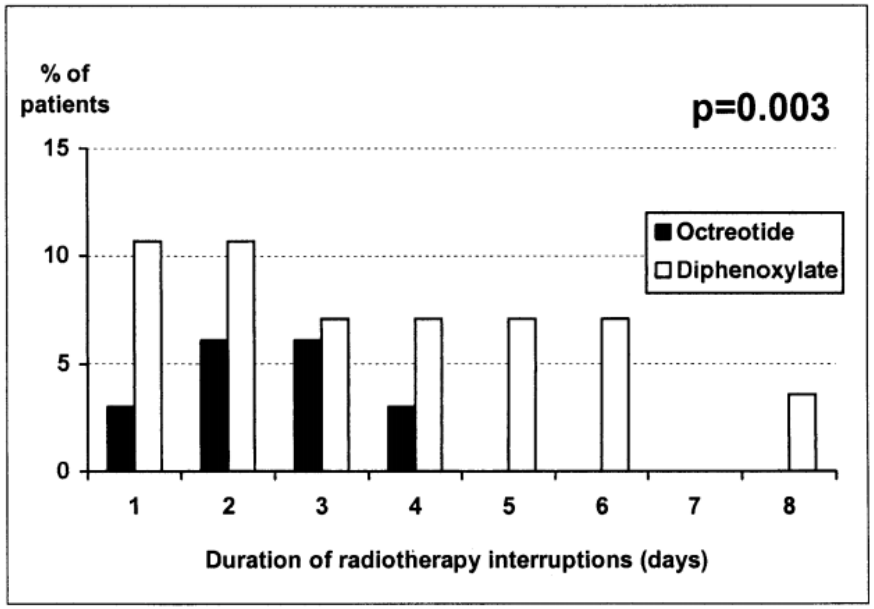


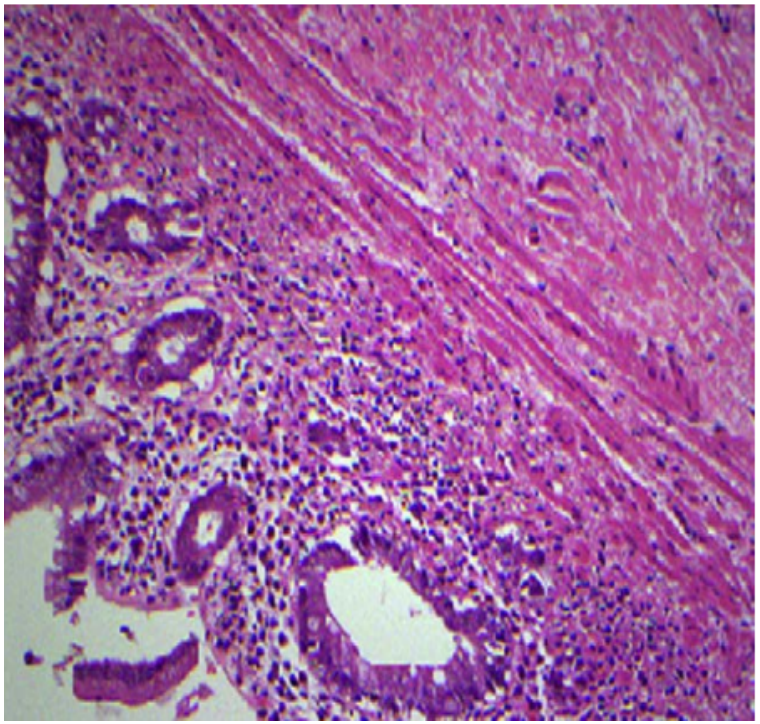

Fig. 2. Duration of radiotherapy interruptions between the two arms.

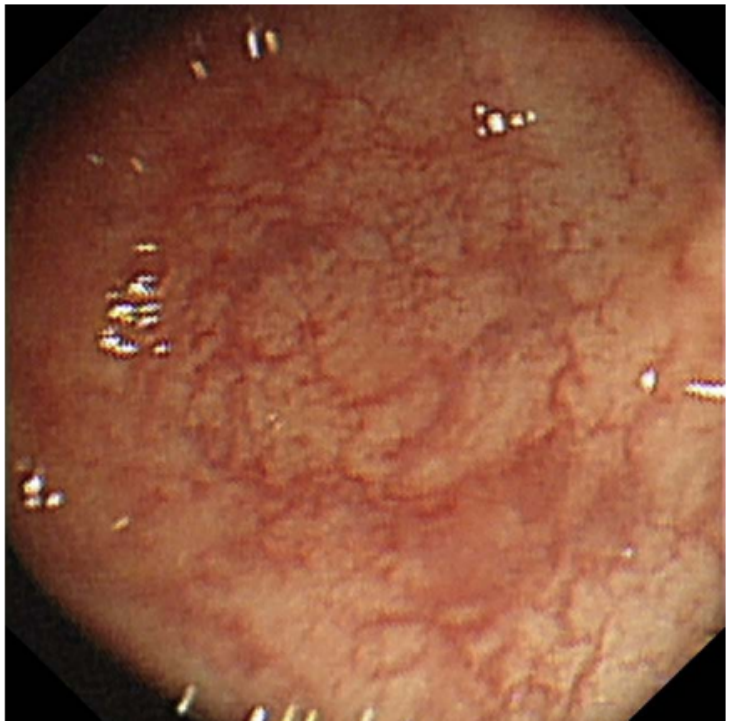
Int. J. Radiation Oncology Biol. Phys., Vol. 54, No. 1, pp. 195–202, 2002

| Diarrea | Terapia | Note |
|---|---|---|
| **Grado 1**<br><4 evacuazioni al giorno | Probiotici, dieta appropriata | monitorare elettroliti, idratazione |
| **Grado 2**<br>4-6 evacuazioni al giorno | Probiotici, dieta appropriata, antidiarroici (loperamide) | monitorare elettroliti, idratazione |
| **Grado 3**<br>≥7 evacuazioni al giorno | Antidiarroici (loperamide), antibiotici, valutare octreotide | monitorare elettroliti, idratazione |
| **Grado 4**<br>Conseguenze potenzialmente letali | Ospedalizzazione | |

**Loperamide** (IMODIUM®, DISSENTEN®)
**Octreotide** (SANDOSTATIN®)

# Enterite Cronica





# Prevenzione

- Stile di vita e Alimentazione
- Prevenzione Farmacologica

Webb et al. j*ournal of Digestive Diseases* 2013 *;* **14;** 350–357

# Stile di vita e Alimentazione

In a retrospective survey of prostate cancer patients treated with radiotherapy, showed increased gastrointestinal symptoms in smokers, overweight and physically inactive men.

Prospective studies evaluating the role of lifestyle intervention in preventing PRD are awaited.

Thomas et al. Clin Oncol (R Coll Radiol 2013;25(4):246e251

# Effects of a dietary intervention on gastrointestinal symptoms after prostate cancer radiotherapy: long-term results from a randomized controlled trial.

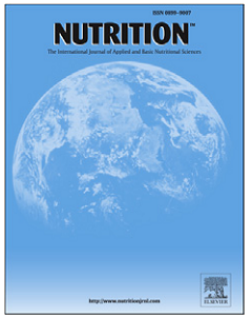

Pts were evaluated for ⩽24months post-radiotherapy

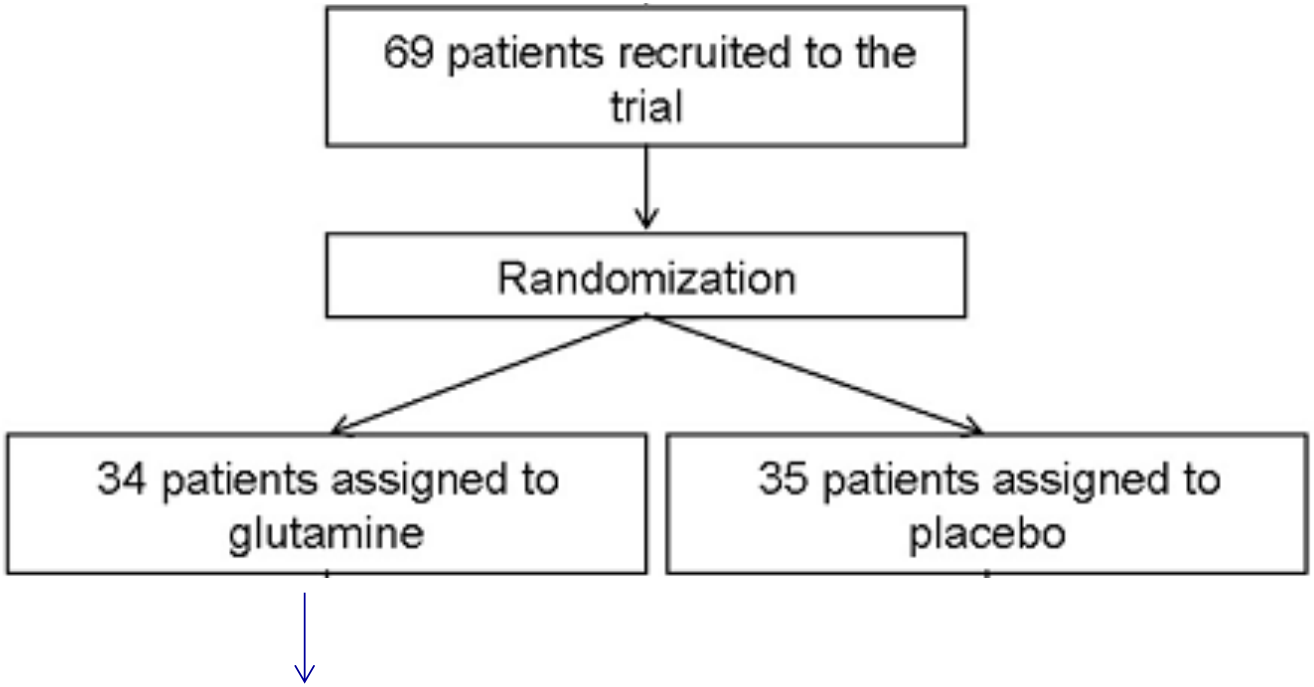
***Conclusion***: *Long-term gastrointestinal symptoms were predominantly mild, and dietary intervention was not superior to a usual diet in preventing these symptoms.*

Petterson et al., Radiother Oncol. 2014 Nov;113(2):240-7

# Effects of oral glutamine during abdominal radiotherapy on chronic radiation enteritis: A randomized controlled trial

Alfonso Vidal-Casariego M.D., Ph.D. [a,*], Alicia Calleja-Fernández R.D., Ph.D. [a],




30 g/d of oral Gln beginning 3 d before starting RT until completion of the antitumoral treatment

Nutrition 31 (2015) 200–204

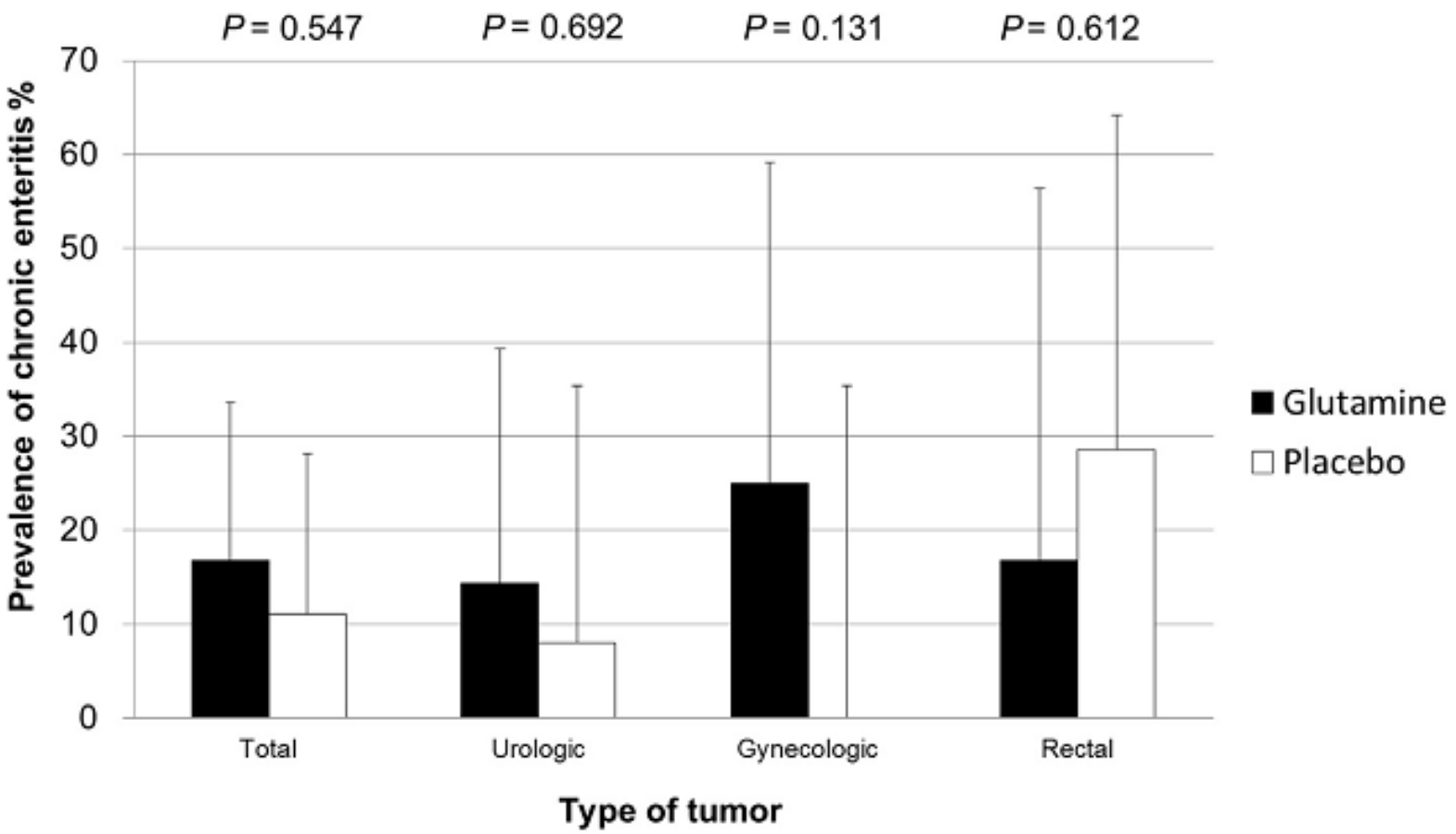



**Fig. 2.** Prevalence of chronic radiation enteritis according to type of tumor.

A. Vidal-Casariego et al. / Nutrition 31 (2015) 200–204

# Prevenzione Farmacologica

## Pentossifillina (TRENTAL ®) e tocoferolo

**Table 3** Studies on therapy of chronic radiation enteritis with tocopherol and pentoxifylline

| author | type of study | patients | symptoms | therapy | result |
|---|---|---|---|---|---|
| Hille A et al. 2005 | retrospective study | 30; 3 – 48 months after pelvic radiation with 45 – 50 Gy | RTOG/EORTC grade 1 – 2: diarrhoea > 5/day, abdominal cramps | -21 with pentoxyfylline 400 mg p. o. 2 × /day, tocopherol 500 mg p. o. 2 × /day for about an average of 10 months<br>-9 symptomatically with NSAID, SAID, loperamide | amelioration in 15 patients, no difference in 6 patients, no aggravation but 3 break offs due to coagulopathy, 3 due to nausea<br>controls: no difference in 6 patients |
| Gothard L et al. 2005 | phase II study, not placebo-controlled | 23 with enteritis/proctitis at least 1 year after high dose pelvic radiation | LENT SOMA scale, at least one grade 3 or 4 disability | Pentoxyfylline 400 mg p. o. 2 × /day, tocopherol 500 mg p. o. 2 × /day over 6 months | no significant amelioration of symptoms or improvement in quality of life scores |

Zimmerer T et al.,Z Gastroenterol 2008; 46: 441–448

# Colestiramina

Resina a scambio ionico che controlla il malassorbimento di acidi biliari, responsabile della diarrea nel 35-72% dei pazienti con Enterite Radioindotta.

Due studi* hanno dimostrato un miglioramento clinico significativo (88% e 73%) in seguito all'assunzione di colestiramina.

La sua scarsa palatabilità rende per difficile il suo utilizzo cronico nei 2/3 dei pazienti

*Andreyev HJ, Int J Radiat Oncol Biol Phys 2005
* Kamal-Bahl SJ, Am J Cardiol 2007

# Loperamide

*Gut* 1993; **34**: 476–482

## Gastrointestinal function in chronic radiation enteritis – effects of loperamide-N-oxide

| *Parameter* | *Placebo* | *Loperamide oxide* | *p Value* |
|---|---|---|---|
| No of subjects | 18 | 18 | |
| Gastrointestinal symptoms: | | | |
| Score | 0 (0–3) | 0 (0–3) | NS |
| Bowel actions/wk | 19 (9–53) | 13·5 (6–39) | <0·001 |
| Stool frequency/3d | 7 (2–14) | 5 (1–10) | <0·05 |
| Stool wt/3d (g) | 450 (186–1275) | 260 (63–1170) | <0·01 |
| Absorption: | | | |
| SeHCAT (%) | 3·3 (0·0–45·7) | 20·5 (0·0–65·4) | <0·01 |
| $^{58}$Co Vit B12 (%) | 74·3 (45·1–100) | 62·8 (37·7–90·9) | <0·05 |
| Faecal fat (mmol/3d) | 33 (11–65) | 33 (9–68) | NS |
| Lactose malabsorption (no) | 10 | 7 | NS |
| Gastrointestinal transit; gastric emptying: | | | |
| Lag phase (min) | 0·5 (0·5–3·5) | 0·5 (0·5–9·5) | NS |
| 50% emptying (min) | 55 (1–160) | 39 (1–135) | <0·01 |
| Small intestinal transit: | | | |
| Start colonic filling (min) | 29 (14–73) | 37·5 (14–135) | <0·01 |
| 50% colonic filling (min) | 125 (83–208) | 164 (83–269) | <0·001 |
| Small intestinal transit (min) | 28 (14–68) | 37 (13–134) | <0·01 |
| Small intestinal residence (AUC) | 27·4 (18·6–46·8) | 41·8 (26·4–62·5) | <0·001 |
| Whole gut transit: | | | |
| First marker (h) | 21·5 (6–45) | 28·5 (10·5–72) | <0·01 |
| 50% markers (h) | 28·5 (10–72) | 58·5 (10·5–72) | <0·05 |
| Intestinal permeability: | | | |
| $^{51}$Cr EDTA (%) | 1·99 (0·091–8·25) | 2·70 (0·16–6·8) | <0·01 |
| Lactulose (mmol/l) | 0·60 (0·04–9·8) | 0·41 (0·07–9·83) | NS |
| Rhamnose (mmol/l) | 1·91 (0·23–52·2) | 2·60 (0·54–21.3) | NS |
| Lactulose/rhamnose (ratio) | 0·06 (0·03–0·25) | 0·06 (0·01–0·28) | NS |

# Camera Iperbarica

# Treatment of gastrointestinal radiation injury with hyperbaric oxygen

**PATIENTS:**
65 patients (37 male, 28 female; mean age 65 years) were treated with HBO2 for radiation damage to the alimentary tract.

**RESULTS**
The response rate was 68%, with a complete and partial response rate of 43 and 25%, respectively

Marshall et al. Undersea Hyperb Med 2007;34: 35–42

# Nutrizione Parenterale

# Role of home parenteral nutrition in chronic radiation enteritis.

30 patients, with mechanical bowel obstruction due to CRE, were retrospectively included in the study and divided in two groups according to the first treatment approach.

17 patients underwent surgery (S group) and 13 patients were supported with HPN

Nutrition autonomy was achieved in 100% and 58.8% of HPN and S group respectively ($p = 0.01$). The overall five-year survival was 90.0% and 68.4% respectively in the HPN and S group ($p = 0.0231$)

Gavazzi C Am J Gastroenterol 2006

# Conclusioni

- Pochi dati circa la prevenzione il trattamento delle enteriti croniche da radiazioni

- Se la diarrea è il sintomo principale, la loperamide può essere efficace

- In casi gravi, con ostruzione o fistole, la nutrizione parenterale a lungo termine sembra essere più efficace della chirurgia

- La Terapia con ossigeno iperbarico sembra essere una buona alternativa terapeutica.

# Amifostine

| Reference | N° Patients | Type of study | Therapy | Acute Toxicities | late toxicity |
|---|---|---|---|---|---|
| ATHANASSIOU Int. J Radiat Oncolo 2003 | 205 | Phase III, multicentric, randomized trial | 340 mg/m2 i.v., 15 min before RT | significant reduction in acute Grade 2–3 bladder and lower GI tract toxicities in the amifostine group ($p < 0.05$, Weeks 3–7). | NS |
| Antonadou et al., Int. J Radiat Oncolo 2004 | 124 | Randomized Phase III Trial | 300 mg/m2 | significantly reduced the incidence of grade 2 gastrointenstinal toxicity | significantly lower incidence of intestinal toxicity |
| Gallardo et al., Int J Gynecol Cancer. 1999 | 20 | Randomized phase II | 825 mg/m2 | No significamt differences | NS |
| Katsanos *et al. Journal of Experimental & Clinical Cancer Research* 2010 | 44 | Randomized phase II | subcutaneously dose of 500 mg. | significant reduction in acute Grade 2–4 bladder and lower GI tract toxicities in the amifostine group ($p < 0.05$, Weeks 3–7). | NS |
| Kligerman MMInt J Radiat Oncol Biol Phys. 1992;22(4):799-802. | 100 | Phase III, multicentric, randomized trial | 340 mg/m$^2$ | significantly reduced the incidence of grade 2 gastrointenstinal toxicity | significantly lower incidence of intestinal toxicity |

## Pharmacological Prevention

In pelvic cancers, 5 small, randomised controlled trials (RCTs) have investigated amifostine

The lack of standardised toxicity end points and adequately powered trials with amifostine are significant limitations in forming firm conclusions of its role in preventing PRD.

The lack of standardised toxicity end points and adequately powered trials with amifostine are significant limitations in forming firm conclusions of its role in preventing PRD

Statins may down-regulate the Rho/ROCK pathway by inhibiting HMG-CoA reductase [Monceau et al., Curr Drug Targets 2010;11(11):1395e1404]

ACEinhibitors may reduce transforming growth factor beta expression [Kharofa J et al., Int J Radiat Oncol Biol Phys 2012;84(1):238e243]

No RCTs have tested these agents and further research is warranted.