



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:

Cenni di patogenesi e strumenti di valutazione

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Radioterapia Oncologica



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BIO-MEDICO
DI ROMA

Radiation Enteritis

Curr Gastroenterol Rep 2014; 16:383

DEEP TISSUE TRAUMATISM FROM ROENTGEN
RAY EXPOSURE.
By DAVID WALSH, M.D. EDIN.,
Physician, Western Skin Hospital, London. W.

Br Med J 1897;2:272-3

Bowel Radiation Injury

Cell Transplantation 2016; 25:1723-46

Radiation Enteropathy

Nat Rev Gastroenterol Hepatol 2014; 11: 470-79

Radiation-induced small bowel disease

Ther Adv Chronic Dis 2014; 5:15-29

An inflammatory process occurring at the level of the small and large intestine as a response to radiation exposure



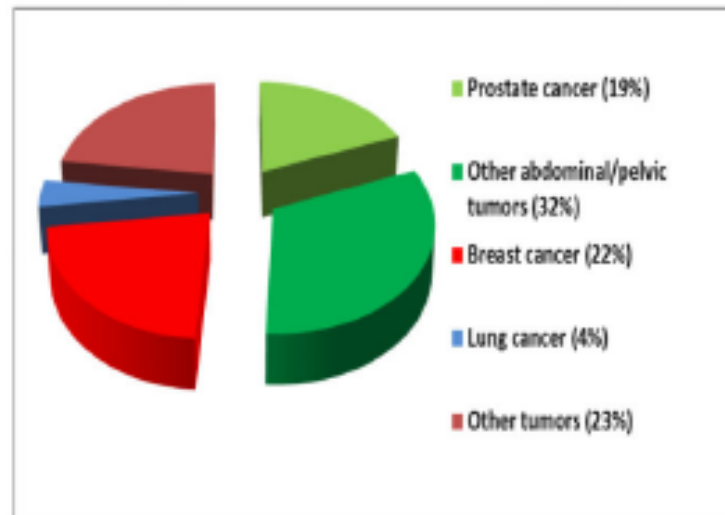
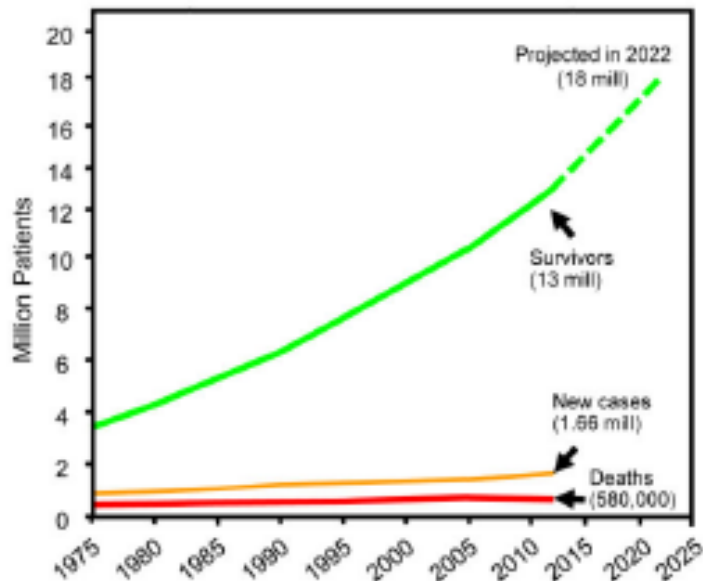
Incidence and prevalence of radiation enteritis

- 60-80% of patients experience temporary symptoms of bowel toxicity during radiation therapy
- 50% of patients who have undergone abdominal or pelvic radiation therapy suffer from some degree of chronic intestinal dysfunction
- The prevalence of radiation enteritis exceeds that of inflammatory bowel disease

Hauer-Jensen M . Nat Rev Gastroenterol Hepatol 2014; 11: 470-79



Magnitude of the clinical problem



The cohort of cancer survivors increases by 3% per year.

Approximately half of all cancer survivors are survivors after abdominal or pelvic tumors

Hauer-Jensen M. Nat Rev Gastroenterol Hepatol 2014; 11: 470-79



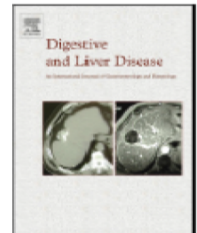


ELSEVIER

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

Digestive and Liver Disease

journal homepage: www.elsevier.com/locate/dld



Oncology

Diarrhoea in irradiated patients: A prospective multicentre observational study

Forty-five Italian radiation oncology departments: 1020 patients

147/1004 (14.6%) patients had diarrhoea

82/147 patients (56.2%) had a drug prescription for diarrhoea. In 63 patients with diarrhoea (43.8%) no drug or dietary measures were administered.

Diarrhoea and Pelvic Irradiation: A Neglected Issue

Poor recognition of symptom diarrhoea among oncologists

Pergolizzi S et al. Dig Liver Dis. 2013;45(11):933-7

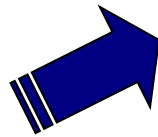
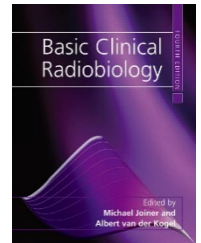
Pergolizzi S et al. Clin Oncol R (R Coll Radiol) 2014;10:669



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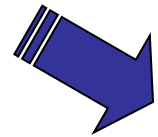
www.unicampus.it

Radiation Enteritis: Pathogenesis



ACUTE:

Inflammation, Cell loss



CHRONIC:

Endoarteritis, Hypoxia, Fibrosis

Joiner & van der Kogel: Basic Clinical Radiobiology



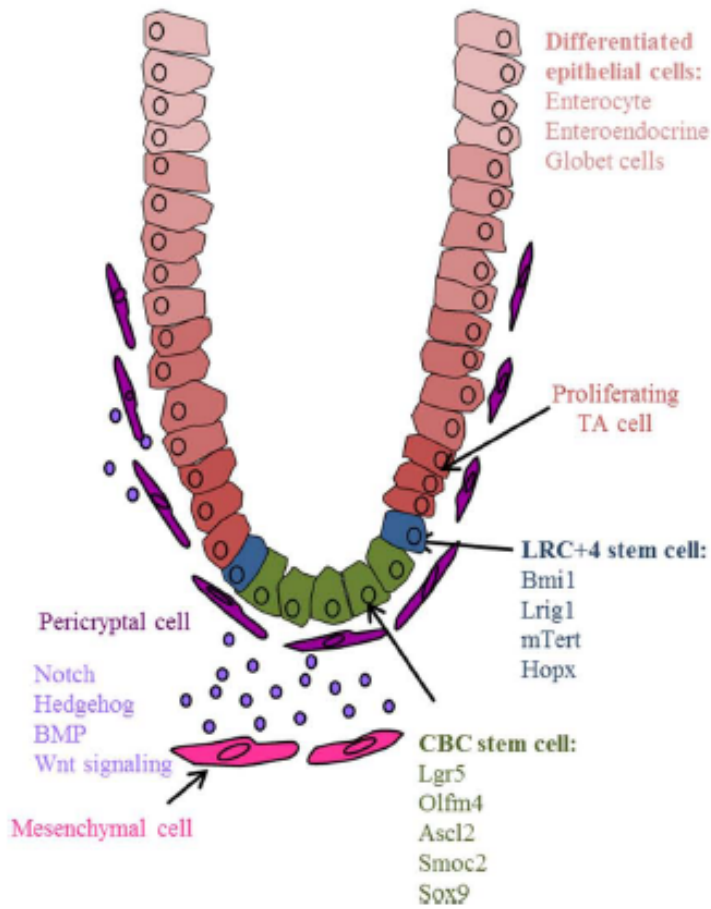
Intestinal Epithelium

Crypts of Lieberkühn

Crypt base columnar (CBC) stem cells

Label-retaining (LR) stem cells

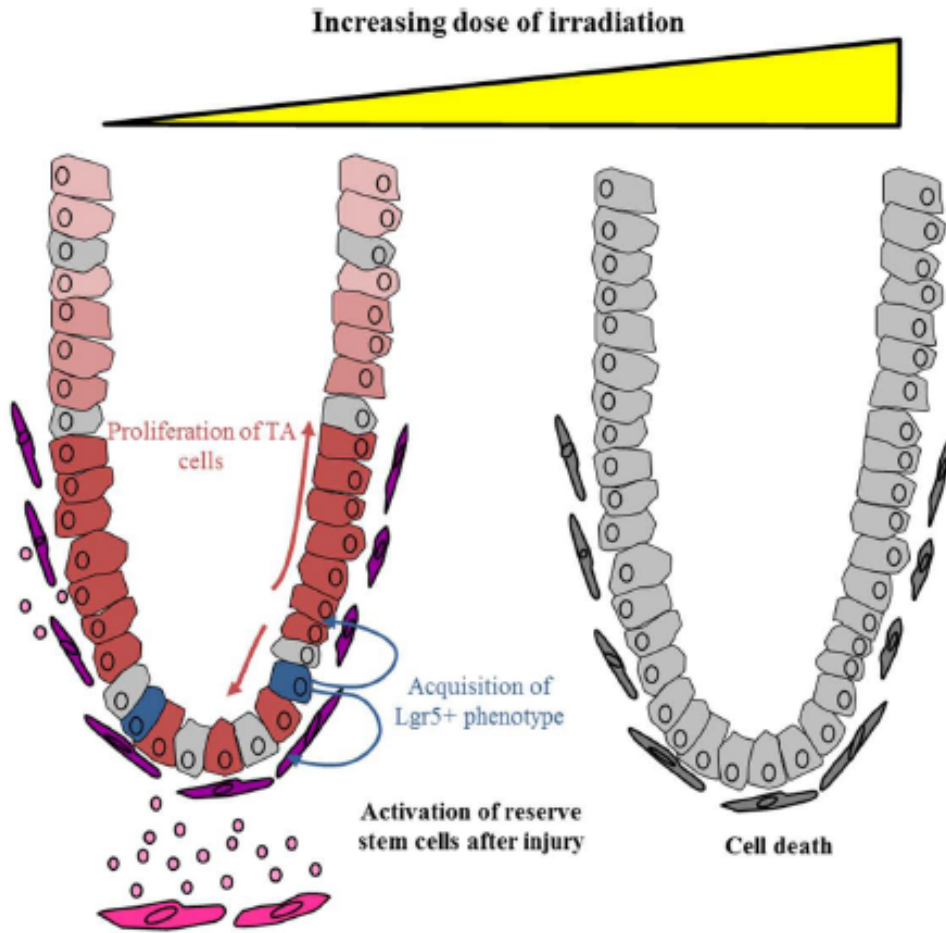
Differentiated epithelial cells



To maintain **the integrity** of the intestinal epithelium ISC must self-renew, proliferate and differentiate to populate the epithelium

Moussa L et al. Cell Transplantation 2016; 25:1723-46

According to the irradiation dose, the number of proliferative cells increase.

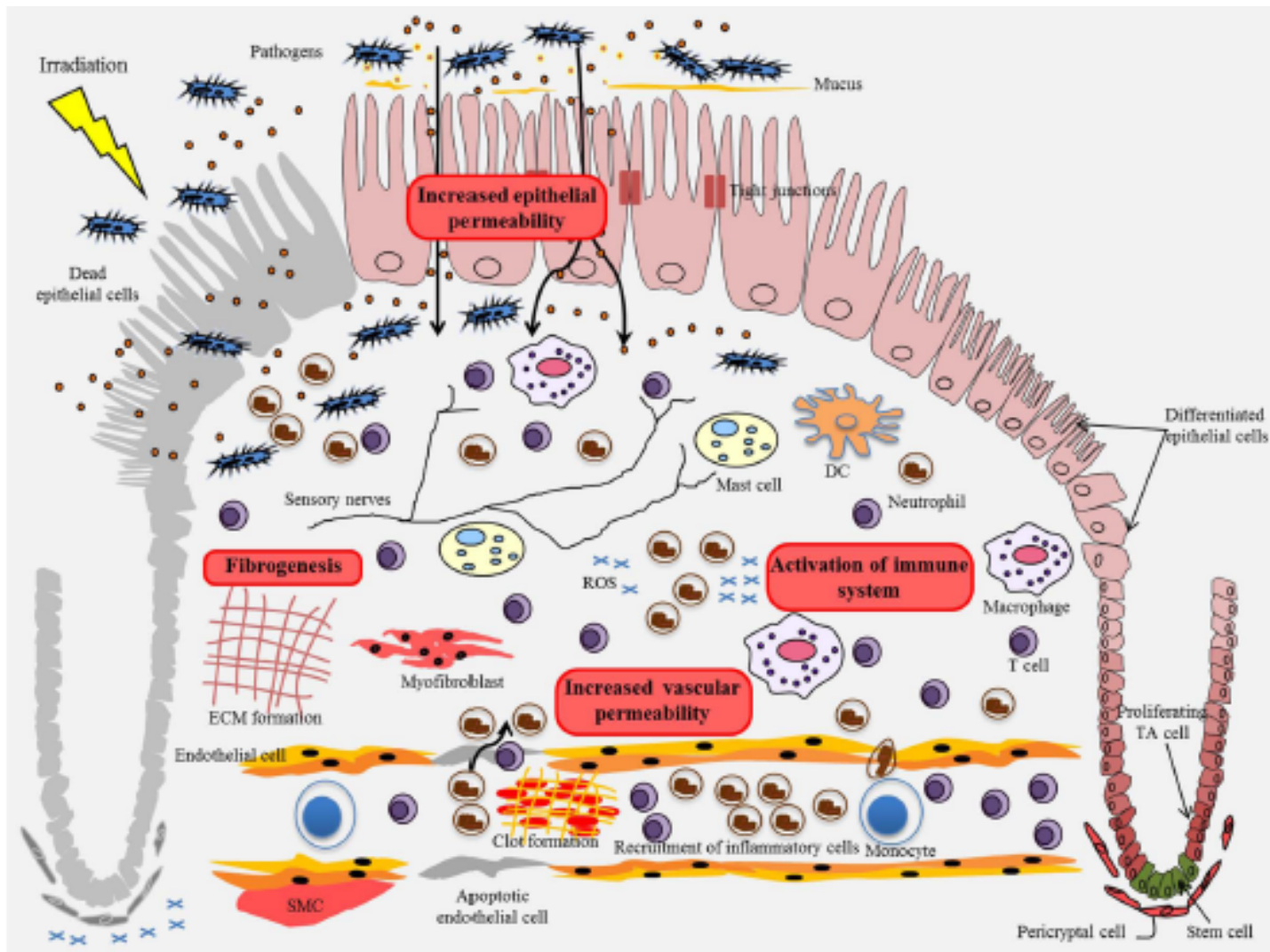


At a dose of irradiation that induce apoptosis of all ISC, the epithelium cannot be renewed.

Moussa L et al. Cell Transplantation 2016; 25:1723-46



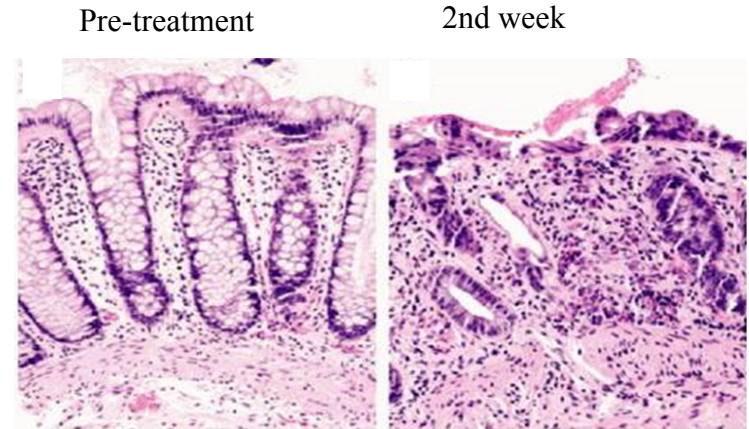
Radio-induced modifications



Radiation Enteritis: Histopathological changes

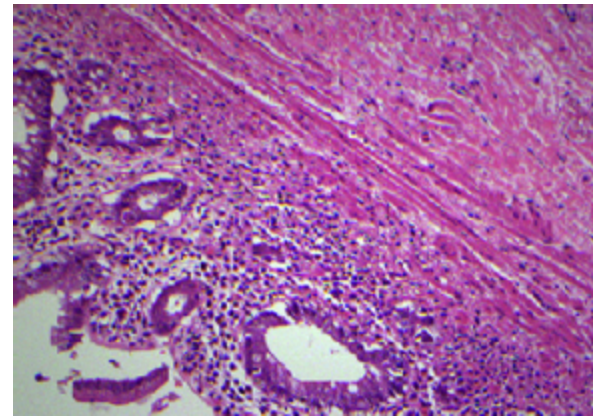
Acute

- Reduced crypt mitoses
- Inflammatory cell infiltrate
- Crypt micro-abscesses
- Epithelial denudation and ulceration

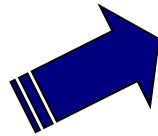


Chronic

- Obliterative endarteritis
- Submucosal fibrosis
- lymphatic dilatation
- Tissue ischemia and necrosis

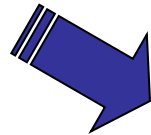


Radiation Enteritis: Symptoms



ACUTE:

*diarrhea, abdominal pain, nausea
and vomiting, anorexia*



CHRONIC:

*diarrhea, abdominal pain, intestinal
obstruction, perforation, malabsorption,
lactose intolerance, weight loss*

Radiation Enteritis: Risk factors

Patient-related factors	Treatment-related factors
Reduced BMI Co-morbidities (diabetes mellitus, hypertension, IBD) Smoking Previous intestinal surgery	Volume of small bowel in radiotherapy fields Radiotherapy dose and fractionation Radiotherapy technique Concomitant chemotherapy use



Toxicity grading scales

SIDE EFFECTS

- RTOG acute radiation morbidity scoring criteria
- RTOG late radiation morbidity scoring scheme
- CTCAE (Common Terminology Criteria for Adverse Events)
- LENT/SOMA score (The Late Effect of Normal Tissue/Subjective Objective Management Analytic)



RTOG acute radiation morbidity scoring criteria

DIARRHEA

Toxicity	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Diarrhea	None	Increase of 2-3 stools/day over pre-Rx	Increase of 4-6 stools/day, or nocturnal stools, or moderate cramping	Increase of 7-9 stools/day or incontinence or severe cramping	Increase of ≥ 10 stools/day or grossly bloody diarrhea, or need for parenteral support

RTOG/EORTC late radiation morbidity scoring scheme

SMALL/LARGE INTESTINE

Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
None	Mild diarrhea; Mild cramping; Bowel movement 5 times daily Slight rectal discharge or bleeding	Moderate diarrhea and colic; Bowel movement >5 times daily; Excessive rectal mucus or intermittent bleeding	Obstruction or bleeding, requiring surgery	Necrosis/ Perforation Fistula



Common Terminology Criteria for Adverse Events (CTCAE)

Version 4.0

Published: May 28, 2009 (v4.03; June 14, 2010)

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health
National Cancer Institute

Gastrointestinal disorders

Adverse Event	Grade				
	1	2	3	4	5
Diarrhea	Increase of <4 stools per day over baseline; mild increase in ostomy output compared to baseline	Increase of 4 - 6 stools per day over baseline; moderate increase in ostomy output compared to baseline	Increase of ≥ 7 stools per day over baseline; incontinence; hospitalization indicated; severe increase in ostomy output compared to baseline; limiting self care ADL	Life-threatening consequences; urgent intervention indicated	Death

Definition: A disorder characterized by frequent and watery bowel movements.

Enterocolitis	Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Abdominal pain; mucus or blood in stool	Severe or persistent abdominal pain; fever; ileus; peritoneal signs	Life-threatening consequences; urgent intervention indicated	Death
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Definition: A disorder characterized by inflammation of the small and large intestines.

List of AE terms commonly encountered in oncology and each AE is accompanied by a grading (severity) scale

CTCAE 4.03 - June 14, 2010



Concluding Remarks

- Current validated objective toxicity grading and PRO reporting tools should be used routinely in the clinic at baseline and follow-up with results acted upon appropriately.
- Effective treatment and prevention are critical to minimizing the burden of this condition.

