



La terapia di supporto in radioterapia oncologica

DISTRETTO ADDOMINALE SUPERIORE

Ernesto MARANZANO
Dipartimento di Oncologia,
S.C. di Radioterapia Oncologica,
Az. Ospedaliera, **Terni**

28 ottobre 2013



Radiotherapy-induced side effects/toxicity

- 1. Prevention of acute (& late) toxicity**
- 2. Treatment/supportive therapy of acute toxicity**
 - a. Organ-specific toxicity (i.e., nausea, vomiting, diarrhea)**
 - b. Evaluation of fatigue, distress & QoL**



Radiotherapy-induced side effects/toxicity

1. Prevention of acute (& late) toxicity

2. Treatment/supportive therapy of acute toxicity

- a. Organ-specific toxicity (i.e., nausea, vomiting, diarrhea)
- b. Evaluation of fatigue, distress & QoL

Gastric perforation following stereotactic body radiation therapy of **hepatic metastasis** from colon cancer

Matthew J. Furman MD ^{a,*}, Giles F. Whalen MD ^a,
Shimul A. Shah MD ^a, Sidney P. Kadish MD ^b

^aDepartment of Surgery, University of Massachusetts Medical School, Worcester, Massachusetts

^bDepartment of Radiation Oncology, University of Massachusetts Medical School, Worcester, Massachusetts



- ✚ Gastric perforation after **SBRT** to a liver metastasis from colon cancer
- ✚ 10 fractions of 5 Gy each for a total of 50 Gy
- ✚ No oral contrast for the delineation of the gastric wall

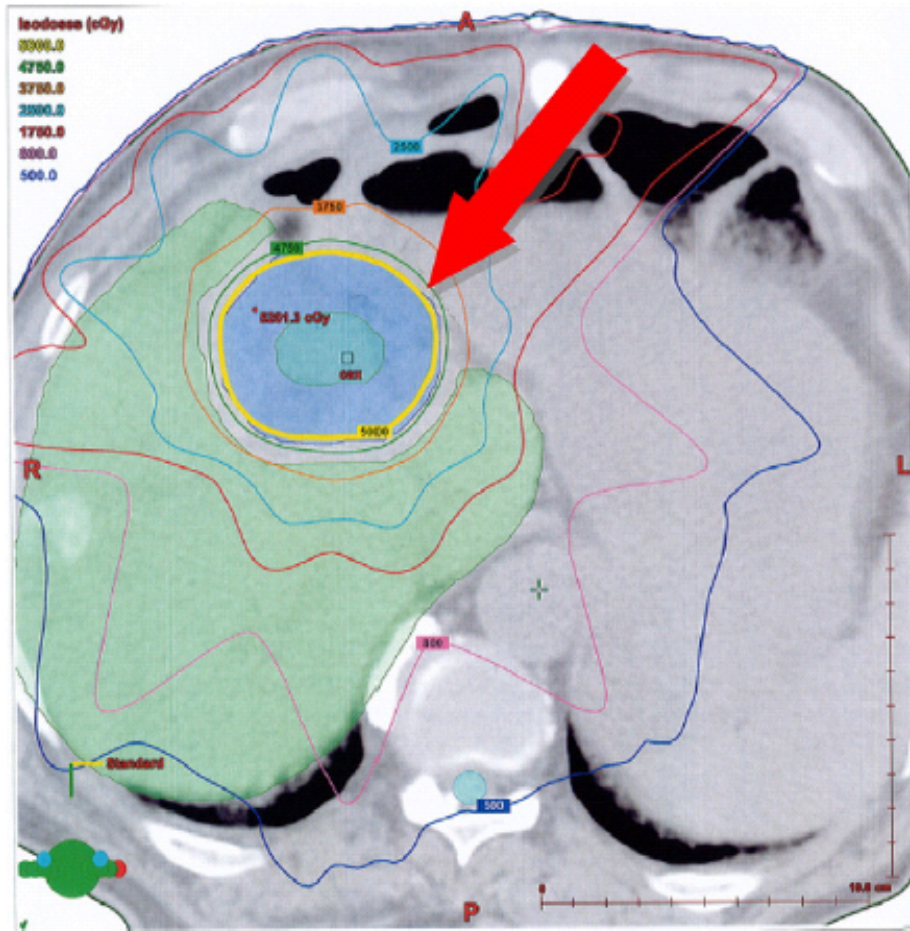


Figure 1 SBRT simulation depicting the suspected gastric wall and hepatic tumor border. The arrow marks the suspected gastric wall and hepatic tumor border. In the absence of oral contrast the delineation of the gastric borders is difficult.

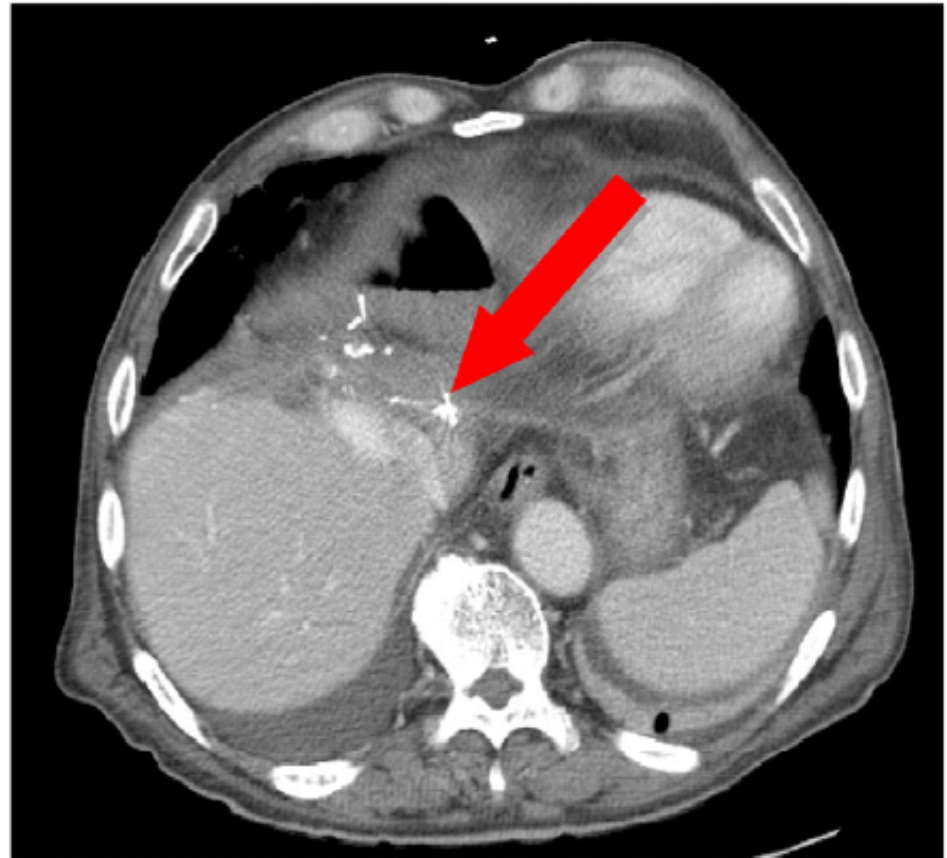


Figure 2 Computed tomography scan depicting the gastrohepatic fistula; surgical clips clearly seen at cut liver edge. The arrow marks the gastrohepatic fistula; surgical clips are clearly seen at cut liver edge.

Commentary

Gastrointestinal stereotactic body radiation therapy requires detailed normal tissue planning to prevent long-term complications

Rachit Kumar MD, Joseph M. Herman MD, MSc*

*Department of Radiation Oncology & Molecular Radiation Sciences, Sidney Kimmel Comprehensive Cancer
Johns Hopkins University School of Medicine Baltimore Maryland*

Stereotactic Body Radiation Therapy for Locally Advanced and Borderline Resectable **Pancreatic Cancer** Is Effective and Well Tolerated

Michael D. Chuong, MD,* Gregory M. Springett, MD, PhD,[†] Jessica M. Freilich, MD,*

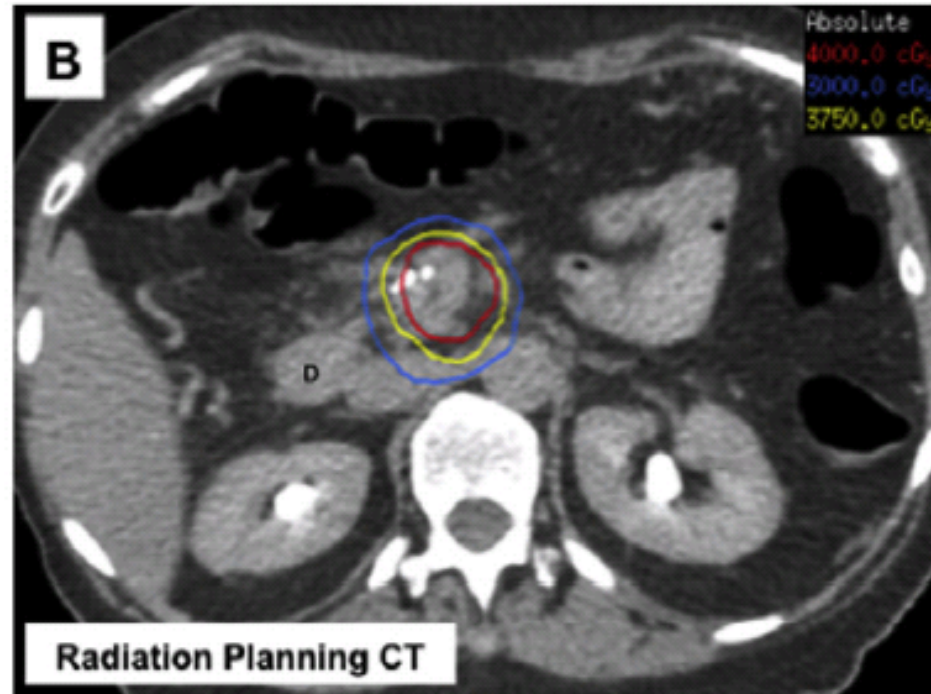
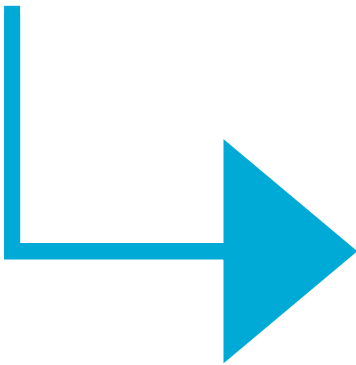
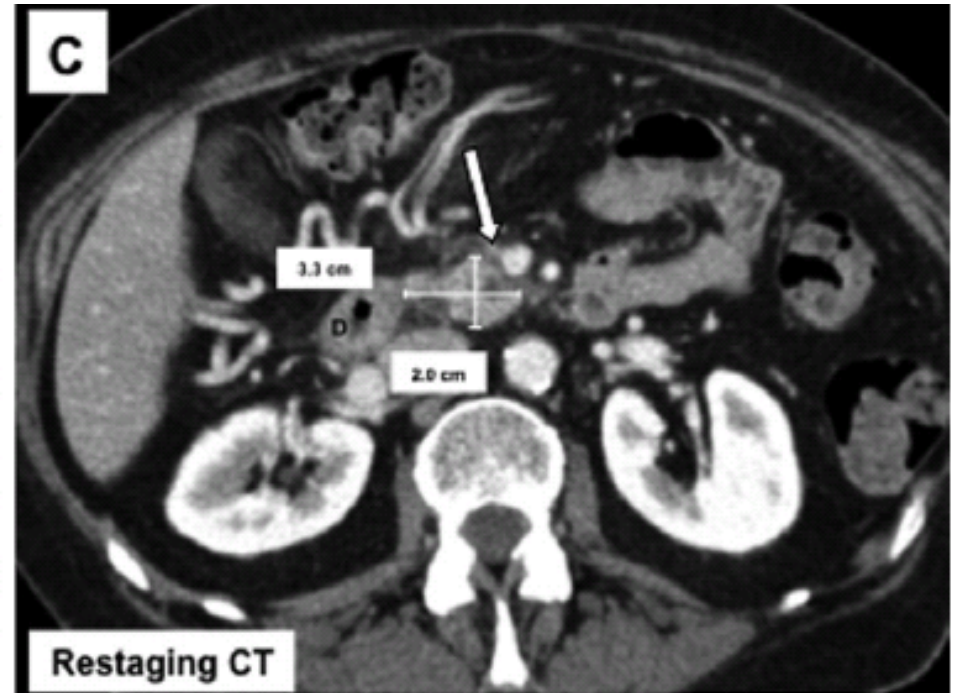
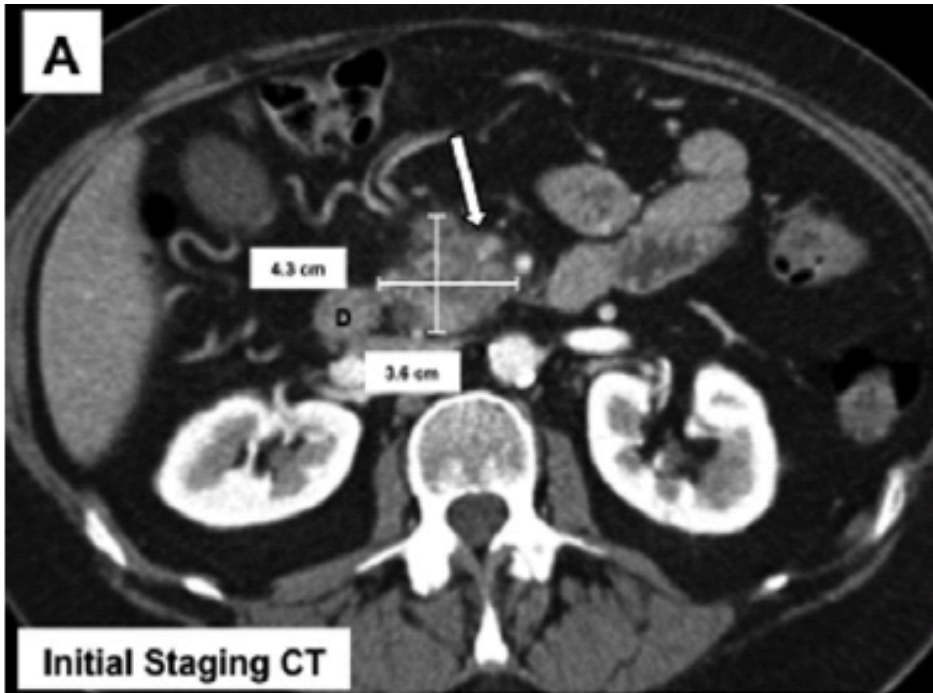
✚ **SBRT** median doses of **35 Gy** and **25 Gy** in 5 consecutive daily fractions were delivered to the region of vessel involvement and the remainder of the tumor, respectively.

Treatment-related toxicity

The most common acute adverse effect was grade 1 to 2 fatigue or nausea. 5% patients experienced late grade 3, GI bleeding or anorexia toxicity

Conclusions:

SBRT safely facilitates margin-negative resection in patients with borderline resectable pancreatic cancer while maintaining a high rate of LC in unresectable patients. These data support the expanded implementation of SBRT for pancreatic cancer.



Stereotactic Body Radiation Therapy for Locally Advanced and Borderline Resectable **Pancreatic Cancer** Is Effective and Well Tolerated

Michael D. Chuong, MD,* Gregory M. Springett, MD, PhD,† Jessica M. Freilich, MD,*

SBRT median doses of 35 Gy and 25 Gy in 5 consecutive daily fractions were delivered to the region of vessel involvement and the remainder of the tumor, respectively.

Treatment-related toxicity

The most common acute adverse effect was grade 1 to 2 fatigue or **nausea**. 5% patients experienced late grade 3, GI bleeding or **anorexia toxicity**

Conclusions:

SBRT safely facilitates margin-negative resection in patients with borderline resectable pancreatic cancer while maintaining a high rate of LC in unresectable patients. These data support the expanded implementation of SBRT for pancreatic cancer.

Bowel Perforation After Radiotherapy in a Patient Receiving Sorafenib

Natascha A.J.B. Peters and Dick J. Richel

Department of Experimental Oncology, Academic Medical Center, Amsterdam, the Netherlands

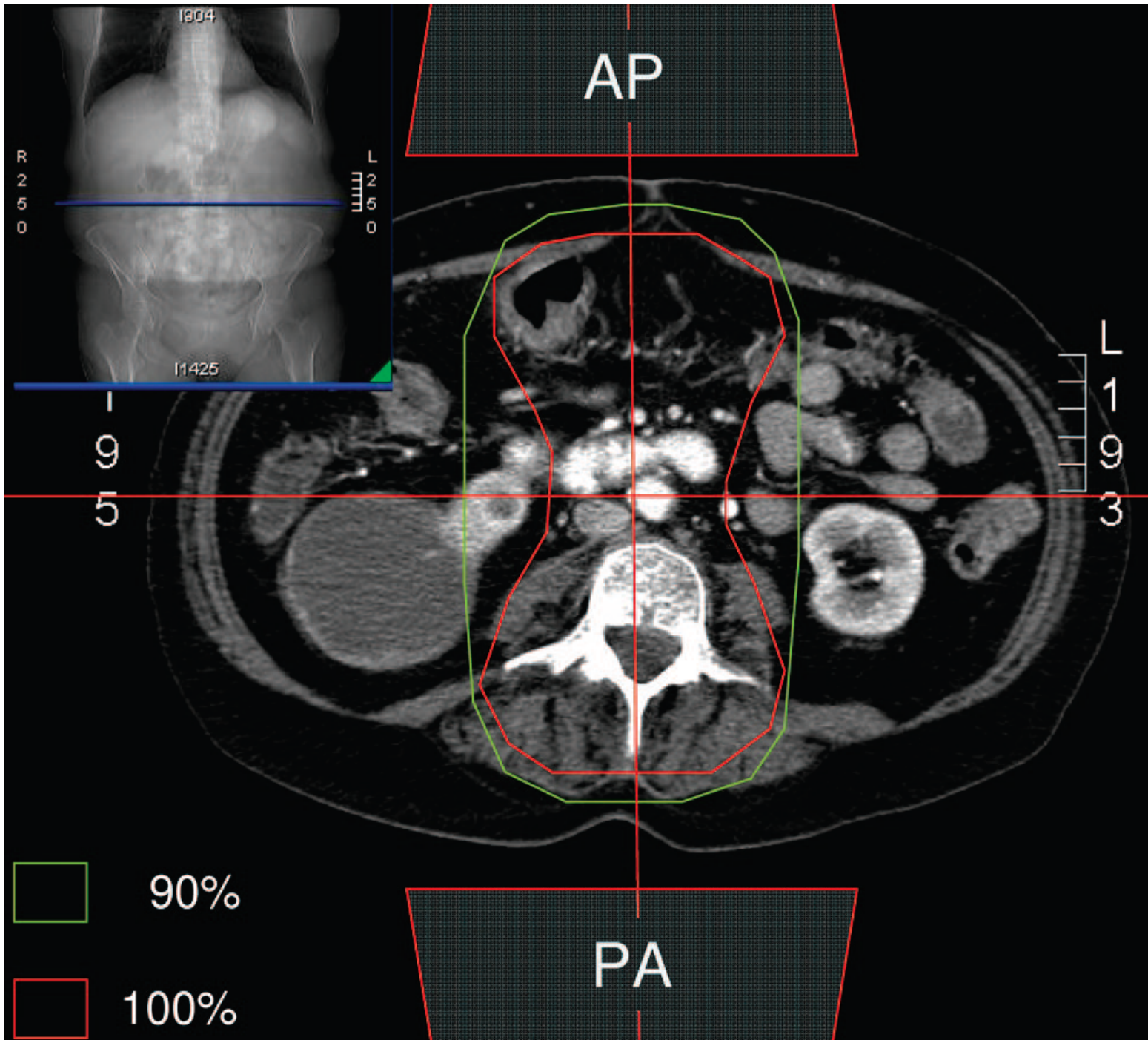
Joost J.C. Verhoeff and Lukas J.A. Stalpers

Department of Radiation Oncology, Academic Medical Center, Amsterdam, the Netherlands

CASE REPORT

Scenario

- ✦ 61-year-old woman with renal cell carcinoma (clear-cell type) and cutaneous metastases.
- ✦ Sorafenib as a first line treatment, 400 mg twice a day.
- ✦ Five weeks later, severe low back pain. At MRI lytic bone metastasis of the L4.
- ✦ Palliative radiotherapy on L3-L5 (8 Gy in one fraction).
- ✦ *Worthy to note*: Sorafenib was stopped 2 days before RT and started again 3 days later.



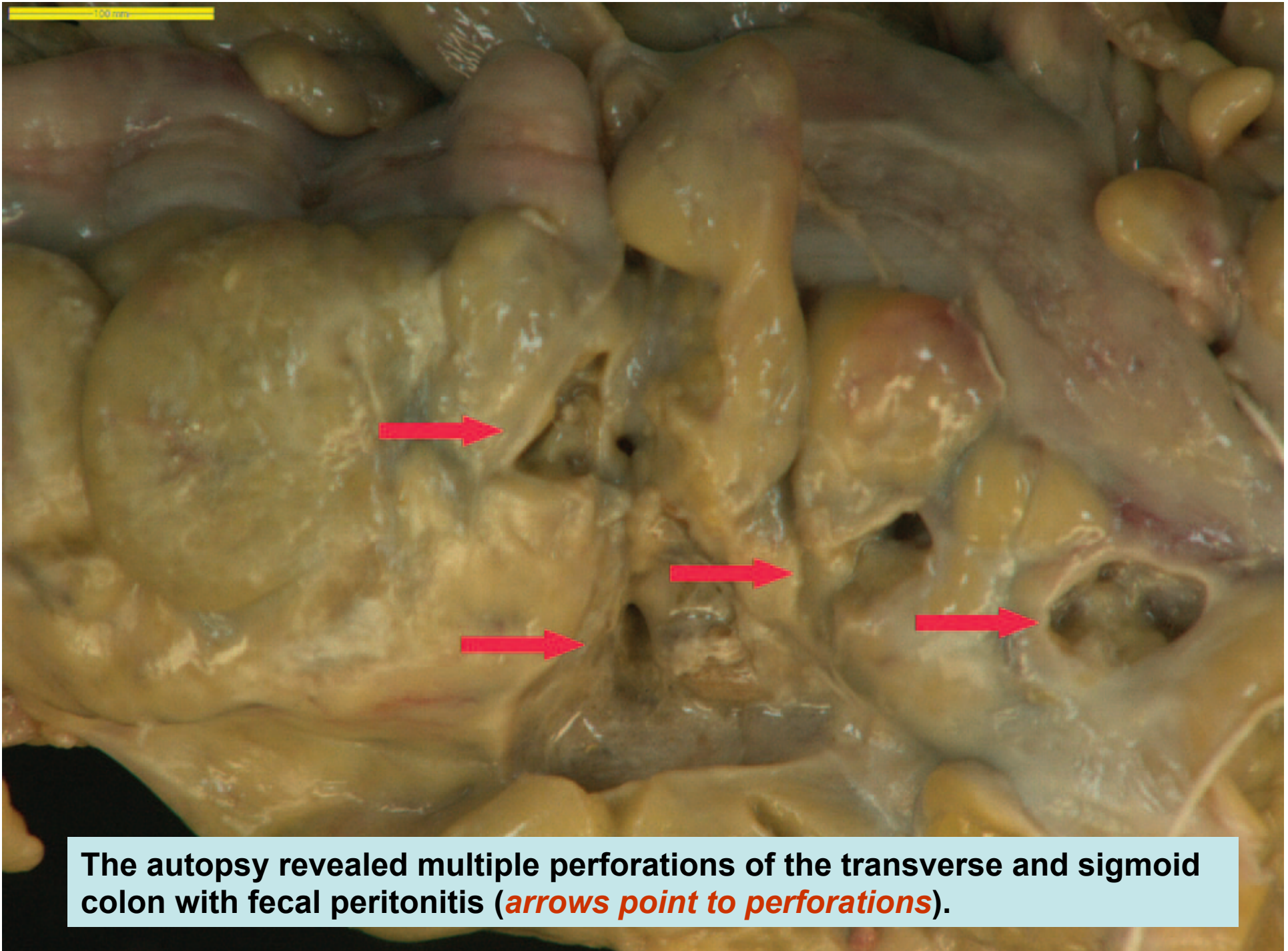
Scenario

+ One week after radiotherapy the patient was admitted to hospital with abdominal pain, diarrhea, and dehydration.

+ She died the next day.

+ The autopsy revealed multiple perforations of the transverse and sigmoid colon with fecal peritonitis.

+ Biopsy specimens of the colon showed ischemic enteritis with radiation-effects and vascular changes with thrombus formation, but no evidence of tumor metastases



The autopsy revealed multiple perforations of the transverse and sigmoid colon with fecal peritonitis (*arrows point to perforations*).

Bowel Perforation After Radiotherapy in a
Patient Receiving Sorafenib

What was the cause/s of this so
severe toxicity?

POSSIBLE CAUSES OF THIS SO SEVERE TOXICITY

✓ Sorafenib?

It could be. Intestinal perforation is reported as a *rare* Sorafenib-induced side effect

✓ Radiotherapy dose?

Probably not. 8-Gy single dose does not exceed the 25 x 2Gy considered the maximum intestinal tolerated dose

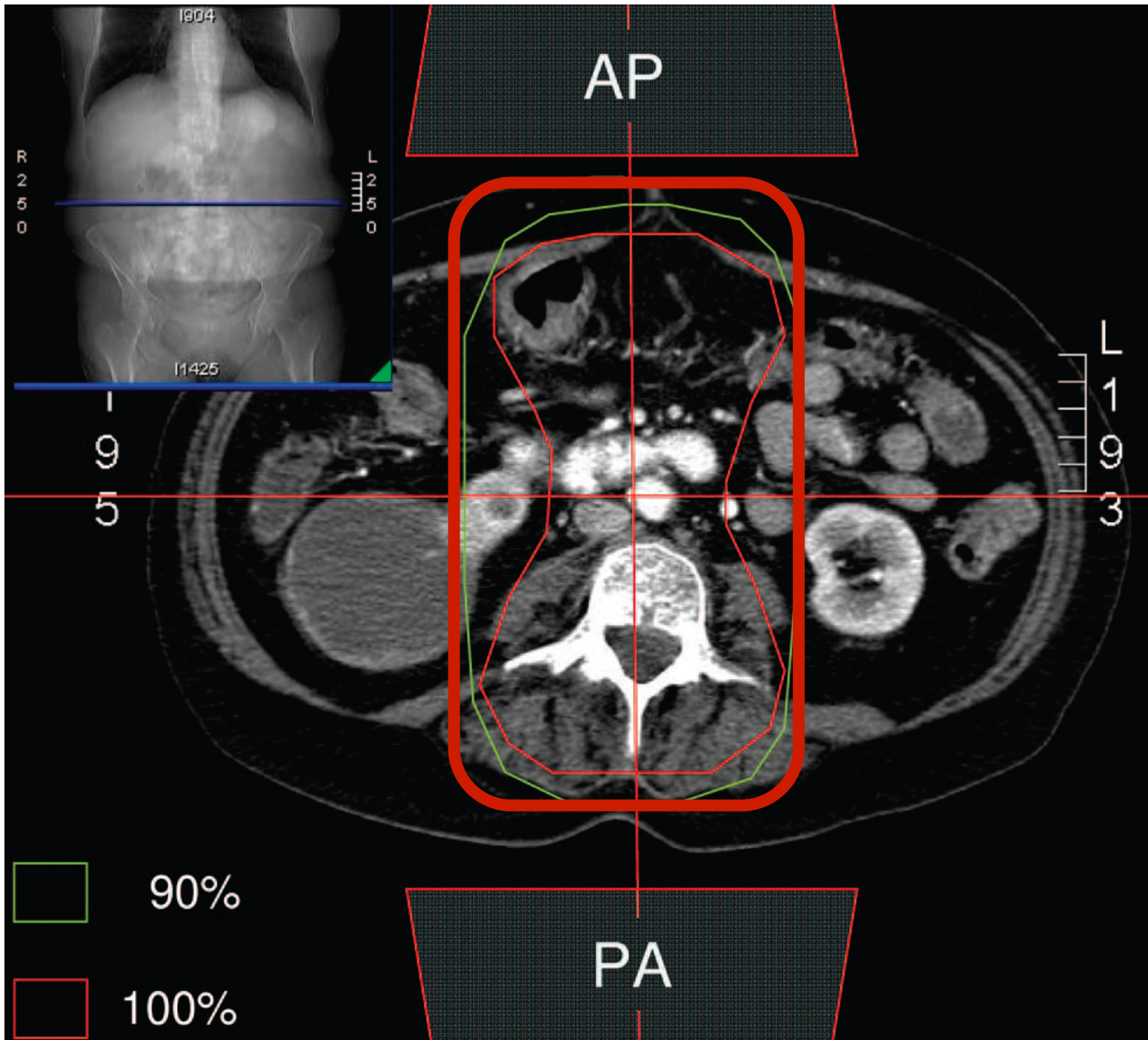
POSSIBLE CAUSES OF THIS SO SEVERE TOXICITY

✓ **Timing of Sorafenib & RT association?**

Probably yes. Too few days between interruption of Sorafenib and RT administration

✓ **Radiotherapy technique?**

Probably yes!





Radiotherapy-induced side effects/toxicity

Prevention of acute (& late) toxicity

Radiation Oncologist is a clinician who:

- ✚ has to prescribe RT using the right technique/technology (in palliative setting too);
- ✚ has to know drugs and their side effects;
- ✚ has to know the previous treatment administered to each patient and suggest the optimal timing between chemo/targeted therapy and RT.



Radiotherapy-induced side effects/toxicity

1. Prevention of acute (& late) toxicity

2. Treatment/supportive therapy of acute toxicity

a. Organ-specific toxicity (i.e., nausea, vomiting, diarrhea)

b. Evaluation of fatigue, distress & QoL

Evidence-based recommendations for the use of antiemetics in radiotherapy

Ernesto Maranzano^{a,*}, Petra Ch. Feyer^b, Alexander Molassiotis^c, Romina Rossi^a,
 Rebecca A. Clark-Snow^d, Ian Olver^e, David Warr^f, Concetta Schiavone^g,
 Fausto Roila on behalf of Participants in the Perugia Consensus Conference 2004

Radiother Oncol. 2005 Sep;76(3):227-33

Table 1. Antiemetic guidelines for management of radiotherapy-induced nausea and vomiting.

Emetic risk level	Site/radiotherapy	Recommendation
<i>MASCC/ESMO</i>		
High	TBI	Prophylaxis with a 5-HT ₃ RA + Dex
Moderate	Upper abdomen, HBI, UBI	Prophylaxis with a 5-HT ₃ RA ± Dex (Dex for days 1–5)
Low	Cranium (all), craniospinal, head and neck, lower thorax, pelvis	Prophylaxis or rescue with a 5-HT ₃ RA
Minimal	Extremities, breast	Rescue with a dopamine RA or a 5-HT ₃ RA



Emesis in radiotherapy

A prospective observational trial on emesis in radiotherapy: Analysis of 1020 patients recruited in 45 Italian radiation oncology centres

Ernesto Maranzano ^{a,*}, Verena De Angelis ^b, Stefano Pergolizzi ^c, Marco Lupattelli ^d, Paolo Frata ^e, Stefano Spagnesi ^f, Maria Luisa Frisio ^g, Giovanni Mandoliti ^h, Giuseppe Malinverni ⁱ, Fabio Trippa ^a, Letizia Fabbietti ^j, Salvatore Parisi ^k, Annamaria Di Palma ^a, Pietro De Vecchi ^l, Costantino De Renzis ^m, Celestino Giorgetti ⁿ, Tiziano Bergami ^o, Roberto Orecchia ^p, Maurizio Portaluri ^q, Marco Signor ^r, Davide Di Gennaro ^s, on behalf of The Italian Group for Antiemetic Research in Radiotherapy – IGARR

✚ **45** Italian radiation oncology centres & **1020** recruited patients

✚ Emesis occurred in **27.9%** patients.

✚ Statistically significant risk factors were concomitant chemotherapy, previous experience of vomiting, irradiated site (**upper abdomen**) and field size (>400 cm²).

✚ An antiemetic drug was given only to a minority (**17%**) of patients receiving RT, and the prescriptions were prophylactic in 12.4% and symptomatic in 4.6%.

✚ **Different** compounds and a wide range of doses and schedules were used

International Patterns of Practice in the Management of Radiation Therapy-induced Nausea and Vomiting

Kristopher Dennis, MD,* Liying Zhang, PhD,* Stephen Lutz, MD,†
Angela van Baardwijk, MD, PhD,‡ Yvette van der Linden, MD,§ Tanya Holt, MBBS,||
Palmira Foro Arnalot, MD,¶ Jean-Léon Lagrange, MD, PhD,** Ernesto Maranzano, MD,††
Rico Liu, MBBS,‡‡ Kam-Hung Wong, MBBS,§§ Lea-Choung Wong, MBBS,|||
Vassilios Vassiliou, MD, PhD,¶¶ Benjamin W. Corn, MD,*** Carlo De Angelis, PharmD,*
Lori Holden, MRT(T),* C. Shun Wong, MD,* and Edward Chow, MBBS, PhD*

Purpose: To investigate **international patterns of practice** in the management of radiation therapy-induced nausea and vomiting (RINV).

Results: In total, **1022 responses** were received. Risk estimates and management decisions for the minimal- and high-risk cases varied little and were in line with guideline standards, whereas those for the low- and moderate-risk cases varied greatly. The serotonin (5-HT₃) receptor antagonists were the most commonly recommended prophylactic agents.

Conclusions: RINV are under-studied treatment sequelae. **New observational and translational studies are needed** to allow for individual patient risk assessment and to refine antiemetic guideline management recommendations.

**International radiation oncology trainee decision making
in the management of radiotherapy-induced nausea
and vomiting**

Kristopher Dennis • Liying Zhang • Stephen Lutz • Yvette van der Linden •
Angela van Baardwijk • Tanya Holt • Jean-Leon Lagrange • Palmira Foro-Arnalot •
Lea-Choung Wong • Ernesto Maranzano • Kam-Hung Wong • Rico Liu •
Vassilios Vassiliou • Benjamin W. Corn • Carlo De Angelis • Lori Holden •
C. Shun Wong • Edward Chow

Results

176 trainees from 11 countries responded.

Only **28 %** were aware of any anti-emetic guideline (!).

Timing and duration of 5-HT₃ receptor antagonist therapy for the prophylaxis of radiotherapy-induced nausea and vomiting: a systematic review of randomized and non-randomized studies

Kristopher Dennis • Leila Makhani •
Ernesto Maranzano • Petra Feyer • Liang Zeng •
Carlo De Angelis • Lori Holden • C. Shun Wong •
Edward Chow

J Radiat Oncol (2013) 2:271–284

Results

Of the 11 high-emetic-risk radiotherapy cohorts:
2, **8 (73%)**, and 1 received 5-HT₃RAs for durations longer than, **equal to**,
or shorter than the **duration of RT**, respectively.

Of the 22 moderate or low-emetic-risk radiotherapy cohorts:
5, **14 (64%)**, and 3 received 5-HT₃RAs for durations longer than, **equal to**,
or shorter than the **duration of RT**, respectively.

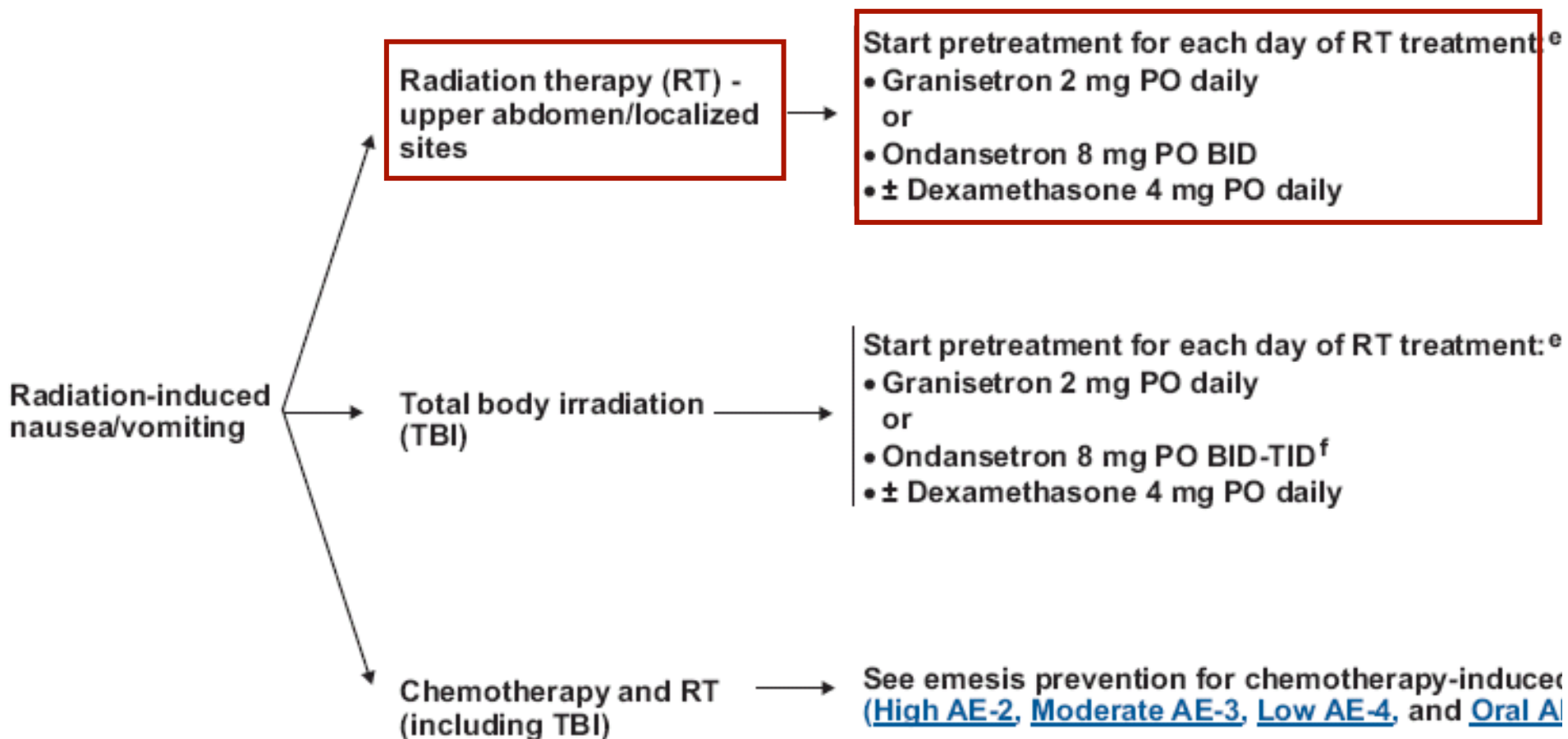
Conclusion

Future studies should compare different timings and durations of therapy with
common efficacy endpoints to develop effective and cost-efficient antiemetic
strategies.

RADIATION-INDUCED EMESIS PREVENTION/TREATMENT

EMETOGENIC
POTENTIAL

TYPE OF RADIATION THERAPY



Diarrhoea in irradiated patients: A prospective multicentre observational study

Stefano Pergolizzi^{a,*}, Ernesto Maranzano^b, Verena De Angelis^b, Marco Lupattelli^b, Paolo Frata^b, Stefano Spagnesi^b, Maria Luisa Frisio^b, Giovanni Mandoliti^b, Pietro Delia^a, Giuseppe Malinverni^b, Fabio Trippa^b, Letizia Fabbietti^b, Salvatore Parisi^b, Pietro De Vecchi^b, Giuseppe Sansotta^a, Celestino Giorgetti^b, Tiziano Bergami^b, Roberto Orecchia^b, Maurizio Portaluri^b, Marco Signor^b, Antonio Pontoriero^a, Anna Santacaterina^b, Davide Di Gennaro^b, On behalf of The Italian Group for Antiemetic Research in Radiotherapy – IGARR

- ✚ **45** Italian radiation oncology centres & **1020** recruited patients
- ✚ **82/147 (14.6%)** pts had diarrhoea. The median minimum number of daily events was 1 (range 1–7) with a median maximum events of 3 (range 1–23).
- ✚ Statistically significant risk factors were concomitant **tumour site (abdomen-pelvis)**, therapeutic purpose and field size (>400 cm²).
- ✚ **82/147 pts (56.2%)** had a drug prescription for diarrhoea
- ✚ **Different** drugs and a wide range of doses and schedules were used

[J Clin Oncol](#). 2004 Jul 15;22(14):2918-26.

Recommended guidelines for the treatment of cancer treatment-induced diarrhea.

[Benson AB 3rd](#), [Ajani JA](#), [Catalano RB](#), [Engelking C](#), [Kornblau SM](#), [Martenson JA Jr](#), [McCallum R](#), [Mitchell EP](#), [O'Dorisio TM](#), [Vokes EE](#), [Wadler S](#).

Common Terminology Criteria for Adverse Events (CTCAE)

Gastrointestinal disorders					
Adverse Event	Grade				
	1	2	3	4	5
Diarrhea	Increase of <u><4 stools</u> per day over baseline; mild increase in ostomy output compared to baseline	Increase of 4 - 6 stools per day over baseline; moderate increase in <u>ostomy output</u> compared to baseline	Increase of <u>>=7 stools</u> per day over baseline; <u>incontinence</u> ; <u>hospitalization</u> 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.

UNCOMPLICATED
CTC grade 1-2 diarrhea
with no complicating
signs or symptoms



1 line

LOPERAMIDE

2 line*

OCTREOTIDE

+ antibiotics

COMPLICATED
CTC grade 3 or 4 diarrhea
or grade 1 or 2 with one or
more of the following signs
or symptoms

- Cramping
- Nausea/vomiting (≥ grade 2)
- Decreased performance status
- Fever
- Sepsis
- Neutropenia
- Frank bleeding
- Dehydration



1 line

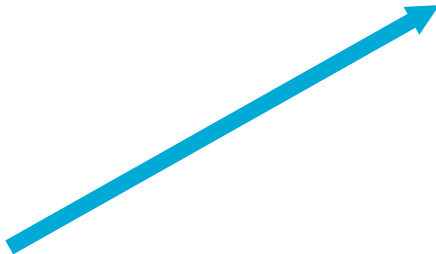
OCTREOTIDE

OSPEDALIZATION

+ antibiotics

+ Idratation

TREATMENT INTERRUPTION



* For RT pts it is recommended to continue with LOPERAMIDE




What to do when you have loose stools (diarrhea)



“Diarrhea kept me from going out and doing things. My nurse told me how important it was to drink more liquids. Drinking more water and avoiding certain foods helped me feel a lot better.”

HOW PREVENT RT-INDUCED DIARRHEA: N.C.I. SUGGESTIONS

These foods and drinks may be easy on your stomach until you feel better:

Soups (clear liquids)	Drinks (clear liquids)	Meals and snacks	Fruits and other foods
<ul style="list-style-type: none">• Clear broth, such as chicken, vegetable, and beef 	<ul style="list-style-type: none">• Clear soda, such as ginger ale• Cranberry or grape juice• Oral rehydration solution drinks, such as Pedialyte®• Tea• Water 	<ul style="list-style-type: none">• Chicken—broiled or baked, without the skin• Crackers• Cream of wheat or rice cereal• Noodles• Oatmeal• Potatoes—boiled, without the skin• Pretzels• White rice• White toast	<ul style="list-style-type: none">• Applesauce• Bananas• Canned fruit, such as peaches and pears• Gelatin (such as Jell-O®) <p>Most canned or cooked fruits and vegetables without seeds or skins are easy on your stomach.</p> 



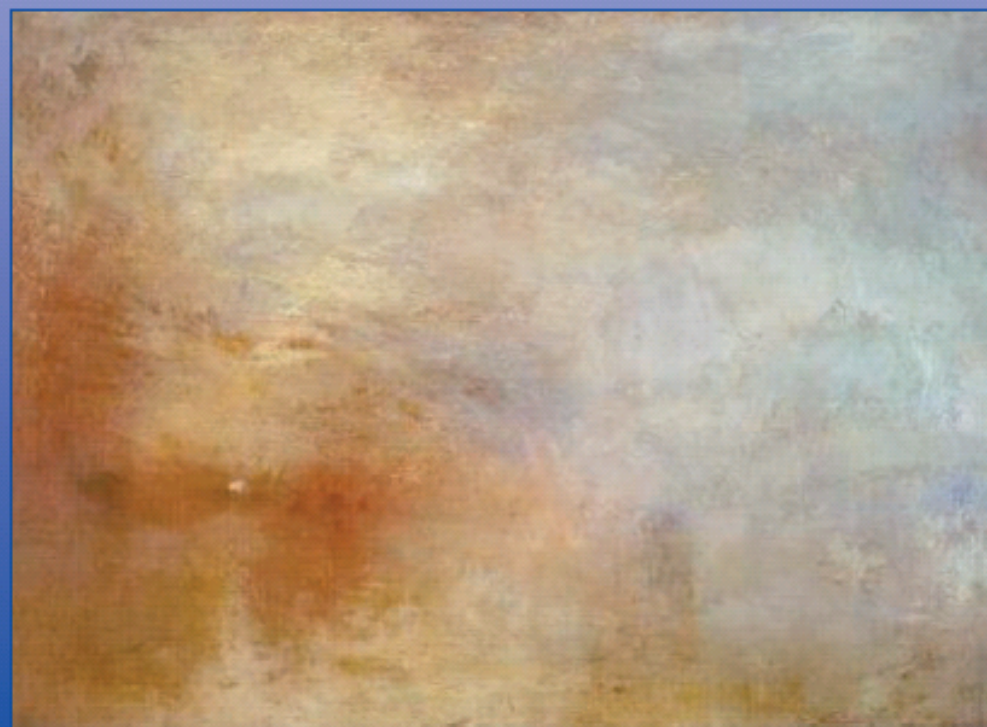
S.C. di RADIOTERAPIA ONCOLOGICA

Direttore: Dr. Ernesto Maranzano

Tel. 0744/205729 - Fax: 0744/205034

LA RADIOTERAPIA ONCOLOGICA

Guida pratica per il malato e i suoi familiari



CIBI PERMESSI

- **Cereali:** Pane bianco, fette biscottate bianche, cracker e grissini comuni, fiocchi d'avena, riso, pasta e semolino
- **Verdure:** Carote, verdura cotta non a foglia, minestre di verdura passata, patate bollite a purea o al forno, zucchine
- **Frutta:** Mele (preferibile frullata e senza buccia), banane e spremute di agrumi
- **Uova:** Altri tipi di cottura
- **Formaggi:** Magri e freschi
- **Carni:** Bianche o rosse purché poco grasse
- **Pesce:** Lesso, al forno o alla brace ma con condimenti leggeri
- **Bevande:** Acqua, camomilla, caffè d'orzo, succhi di frutta, yogurt, succo di limone
- **Dolci:** dolci poco elaborati e poco grassi, crostate, biscotti non integrali, gelati alla frutta

LA RADIOTERAPIA DELL'ADDOME

Gli effetti collaterali più frequenti del trattamento radiante sull'addome sono rappresentati da nausea, vomito e diarrea. Questi sono tanto più importanti quanto più ampia è la zona irradiata.

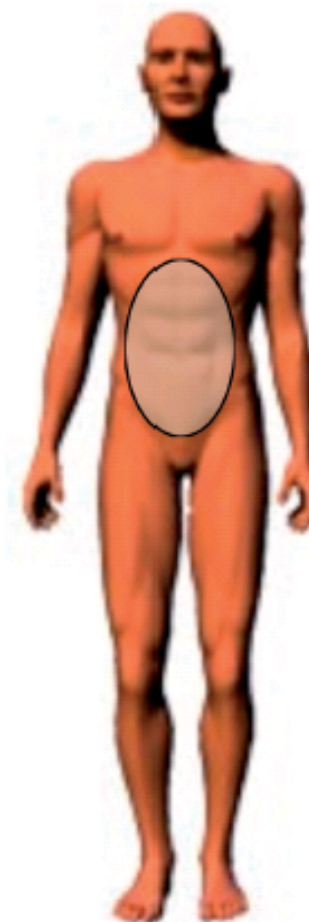
Nausea e/o vomito

Se il paziente ha nausea e/o vomito, deve cercare di fare pasti piccoli e frequenti, mangiare cibi asciutti, non dovrebbe bere durante i pasti ma circa un'ora prima o dopo. Deve poi evitare odori che potrebbero aumentare il senso di nausea.

Il medico, se necessario, potrà risolvere questo disturbo con l'aiuto di farmaci.

Diarrea

Il paziente deve essere correttamente informato sul tipo di alimentazione da seguire prima di iniziare il trattamento, poiché ciò può ridurre sensibilmente l'entità di tale disturbo. In particolare si consiglia di bere circa 1,5-2 litri al giorno di liquidi per mantenere idratato il corpo.



Disturbi urinari

La radioterapia sull'addome può causare con una certa frequenza disturbi urinari; il paziente può infatti avere la necessità di urinare più spesso anche con urgenza, accusare bruciore e senso di pressione o di corpo estraneo oppure uno stimolo continuo ad urinare. Anche in questo caso è importante bere molto (circa 1,5-2 litri di liquidi al giorno).

Attività sessuale

Durante il ciclo di radioterapia, il paziente potrà notare dei cambiamenti nella sua attività sessuale, specie una riduzione del desiderio e della potenza. Questi disturbi variano molto da persona a persona, hanno spesso una componente psicologica e sono limitati al periodo di trattamento.

SUGGERIMENTI DIETETICI PER PAZIENTI IRRADIATI SULL'ADDOME

In genere evitare cibi fritti o soffritti, sughi grassi o piccanti, spezie come pepe e peperoncino, cacao

CIBI DA EVITARE

- **Cereali:** tutti i cereali integrali (pane, fette biscottate, biscotti o cracker)
- **Verdure:** insalate crude, legumi, carciofi, catalogna, cime di rape, bietola, spinaci, cavoli, cavolfiori, broccoli
- **Frutta:** prugne, fichi, fragole, mirtilli, lamponi, ribes, mele cotogne, more, noci, nocciole, datteri, mandorle, pinoli, avocado, cocco fresco, tutta la frutta secca
- **Uova:** fritte, frittate
- **Formaggi:** piccanti e molto grassi o stagionati
- **Carni:** maiale nelle sue parti più grasse, insaccati, frattaglie, trippa, carni affumicate
- **Pesce:** anguilla e pesce grasso in genere, frutti di mare e fritture
- **Bevande:** gasate, fredde, caffè, latte, cioccolato, alcoliche
- **Dolci:** creme, dolci a base di frutta secca e fresca, panna, cacao, gelati di crema

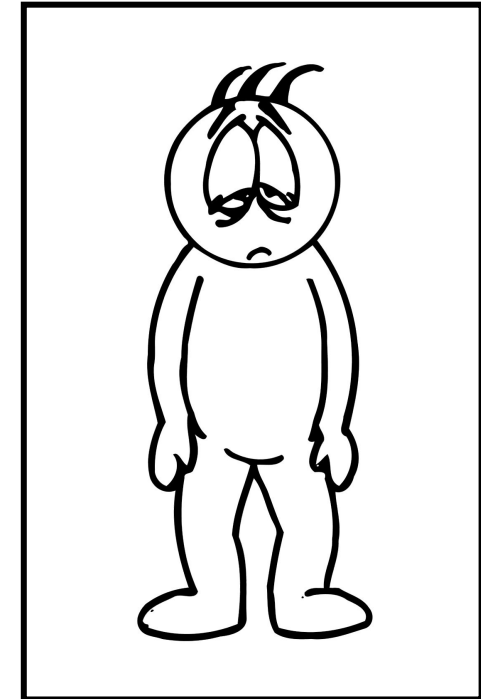


Radiotherapy-induced side effects/toxicity

1. Prevention of acute (& late) toxicity
2. Treatment/supportive therapy of acute toxicity
 - a. Organ-specific toxicity (i.e., nausea, vomiting, diarrhea)
 - b. Evaluation of fatigue, distress & QoL**

What Is FATIGUE?

It is an illness characterized by prolonged, debilitating, **weakness** severe enough to affect one or more aspects of a person's life. It is also characterized by multiple nonspecific symptoms such as **headaches**, recurrent **sore throats**, **muscle/joint pains**, **memory and concentration difficulties**.



European Journal of Cancer (2013) **49**, 1957–1966

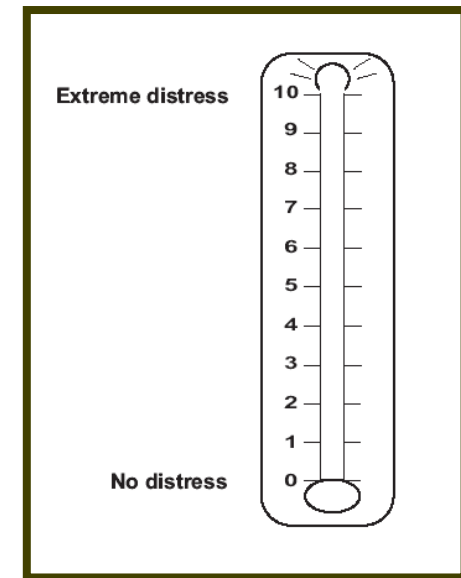
Quantifying fatigue in (long-term) colorectal cancer survivors:

A study from the population-based Patient Reported Outcomes Following Initial treatment and Long term Evaluation of Survivorship registry

Melissa S.Y. Thong^{a,b,*}, Floortje Mols^{a,b}, Xin S. Wang^c, Valery E.P.P. Lemmens^{b,d},
Tineke J. Smilde^e, Lonneke V. van de Poll-Franse^{a,b}

What Is DISTRESS?

Distress is a multifactorial unpleasant emotional experience of a **psychological** (cognitive, behavioral, emotional) and/or **spiritual nature** that may interfere with the ability to cope effectively with cancer, its physical symptoms and its treatment



Support Care Cancer (2013) 21:1043–1051
DOI 10.1007/s00520-012-1624-3

ORIGINAL ARTICLE

Psychological distress in cancer patients undergoing radiation therapy treatment

L. J. Mackenzie • M. L. Carey • R. W. Sanson-Fisher •
C. A. D'Este

Gastric cancer

QoL

Pancreatic cancer

Contents of the EORTC QLQ-STO22

Multi-item scales

Dysphagia/odynophagia

- Eating solid food
- Eating soft or liquidised food
- Drinking liquids
- Discomfort when eating

Pain/discomfort

- Pain in stomach area
- Discomfort in stomach area
- Abdominal bloating

Dietary restrictions

- Early satiety
- Enjoying meals
- Eating slowly
- Change in taste
- Trouble eating in front of others

Upper gastro-intestinal symptoms

- Reflux
- Acid indigestion/heartburn
- Trouble belching

Specific emotional problems

- Thinking about their illness
- Worry about weight loss
- Worry about future health

Single items

- Having a dry mouth
 - Body image
 - Hair loss (two questions)
-

Table 2. Content of the EORTC QLQ-PAN26

Pain	Body Image
Abdominal discomfort	Physical attractiveness
Back pain	Satisfaction with body
Position related pain	
Night time pain	
Eating related items	Side effects
Restriction of diet intake	Burden of treatment
Restriction of food types consumed	Dry mouth
	Taste changes
Indigestion	Fear of future health
Flatulence	Ability to plan future
Cachexia	Health care satisfaction
Loss of muscle strength	Information
Weight loss	Support
Hepatic	Altered bowel habit
Jaundice	Frequency of elimination
Pruritus	Urgency of elimination
Ascites	Sexuality
Swollen abdomen	Sexual interest
	Sexual enjoyment

A three-masted sailing ship with white sails is shown navigating through a stormy sea. The sky is dark blue with white clouds and a bright lightning bolt striking down. The ship is tilted slightly to the right, and the water is dark and turbulent. The overall scene conveys a sense of danger and struggle.

DISTRESS

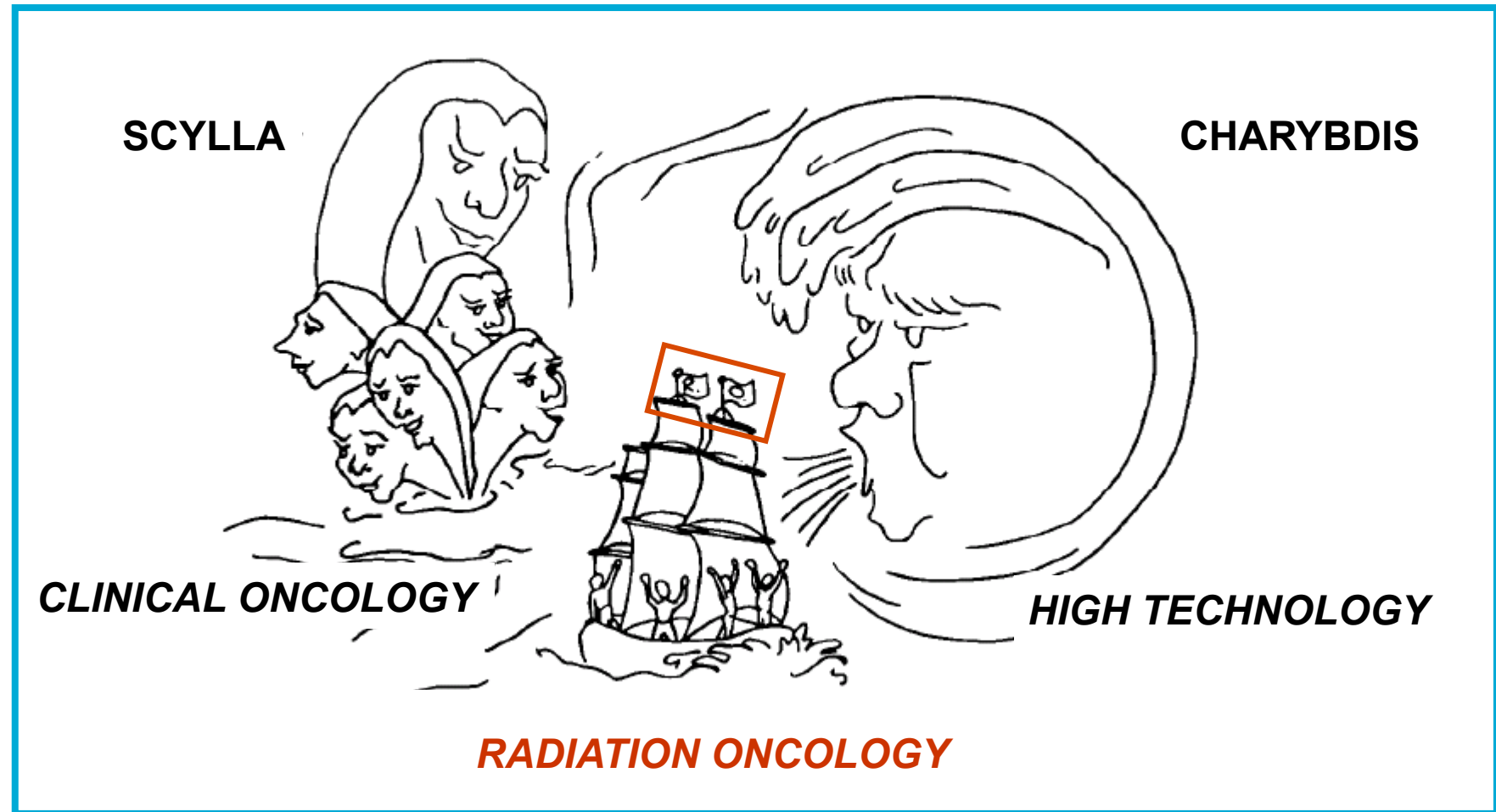
FATIGUE

QoL

CLINICAL ONCOLOGY

HIGH TECHNOLOGY

My wishful thinking



Radiation Oncology will direct successfully between clinic (Scylla) and technology (Charybdis), and will survive as an independent discipline

P. Rubin, ASTRO 1980, modified