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Reirradiation for Gastrointestinal Tumors

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Re-RT in GI TUMORS

- RECTUM
- PANCREAS
- ESOPHAGUS
- ABDOMINAL LYMPH NODE metastases or oligo-recurrence

TOPICS

- Indications of Re-RT: careful pts selection !
- Identify different dose fractionations & technique
- Outcome measures of RE-RT

MUST !!!
Declare the AIMS !!!

- Curative intent ???
- Loco-regional control
- Quality of life symptom control
- Part of Clinical study

- Biopsy confirmation
- Informed consent for risks of RE-RT
- No significant tox from previous RT
- Radiosensitive tumor

.....Calculating EQD2

$$EQD_2 = D \cdot \frac{d + (\alpha/\beta)}{2 + (\alpha/\beta)}$$

D = dose totale
d = dose/fz

Vdose (fz convenzionale) ⟹ Vdose (fz non convenzionale)

$$D = EQD_2 \cdot \frac{2 + (\alpha/\beta)}{d + (\alpha/\beta)}$$

$$\text{Dose Constraints}_{\text{non convenzionale}} = \text{Dose Constraints}_{\text{convenzionale}} \cdot \frac{2 + (\alpha/\beta)}{d + (\alpha/\beta)}$$

Table 4. Re-RT recommendations based on site specific case scenarios

Site/tumor	Common Re-RT techniques (in descending order)	Common dose–fractionations (in descending order)
GIT	3D-CRT, conventional RT, SRS, IMRT	30–40 Gy/15–20 fx, 30.6 Gy/17 fx, 25 Gy/10 fx, 30 Gy/10 fx* Less common regimens: 35 Gy/15 fx, 20 Gy/5 fx* or 8 Gy/1 fx

Radiation Oncology

Radiation Oncology 2009, **4**:55

BioMed Central

Short report

Open Access

Reirradiation to the abdomen for gastrointestinal malignancies

Waqar Haque[1], Christopher H Crane[1], Sunil Krishnan[1], Marc E Delclos[1], Milind Javle[2], Christopher R Garrett[2], Robert A Wolff[2] and Prajnan Das*[1]

toxicity. Abdominal reirradiation appeared to provide local control, albeit with a limited duration. We suggest that abdominal reirradiation could have many potential applications in selected patients with recurrent or metastatic gastrointestinal cancers. Reirradiation may help in palliation of symptoms, such as pain or bleeding. In

Curative setting

- **R0 resection: 39-89%**
- **Median SVV: 39-60 months in resected pts**
  12-16 months in palliative pts

Palliative setting

- **Complete o partial pain relief: 83-94%**
- **Rectal bleeding completely resolved: 100%**
- **Partial o complete symptom relief: >80%**

The rationale for hyperfractionated, accelerated therapy is that small fraction doses increases the therapeutic ratio by exploiting the difference in fractionation sensitivity between tumour (high α/β) and late-reacting normal tissue (low α/β) [33]. Reirradiation doses can be recalculated to equivalent doses delivered with 2 Gy fractions (EQD_{2Gy}) for comparison of fractionation schemes ($EQD_{2Gy} = n * d * ((d + \alpha/\beta)/(2 + \alpha/\beta))$).

Summary

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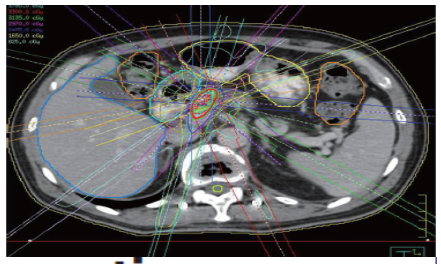
Systematic Review

Reirradiation of locally recurrent rectal cancer: A systematic review

Marianne Grønlie Guren [a,b,*], Christine Undseth [a], Bernt Louni Rekstad [c], Morten Brændengen [a], Svein Dueland [a], Karen-Lise Garm Spindler [d], Rob Glynne-Jones [e], Kjell Magne Tveit [a,b,f]

[a] Department of Oncology; [b] K.G.Jebsen Colorectal Cancer Research Centre; [c] Department of Medical Physics, Oslo University Hospital, Norway; [d] Department of Oncology, Aarhus University Hospital, Denmark; [e] Centre for Cancer Treatment, Mount Vernon Hospital, Northwood, UK; [f] University of Oslo, Norway

- **Re-RT: feasible, safe and effective for radical resection or palliation**
- **Curative intent: hyperfx RT-Chemo + S**
- **Similar results with RE-RT+S+IORT**
- **Few experiences with hyperthermia and brachytherapy combination; limited data for SBRT**
- **Experienced centres; prospective trials**
- **Palliative intent: once-daily RE-RT (1.8/3Gy/die)**



Review Article on Pancreatic Cancer

Advances of stereotactic body radiotherapy in pancreatic cancer

Chin J Cancer Res 2015;27(4):349-357

Qichun Wei[1], Wei Yu[1], Lauren M. Rosati[2], Joseph M. Herman[2]

J Gastrointest Oncol 2013;4(4):343-351

Re-irradiation with stereotactic body radiation therapy as a novel treatment option for isolated local recurrence of pancreatic cancer after multimodality therapy: experience from two institutions

Aaron T. Wild[1*], Susan M. Hiniker[2*], Daniel T. Chang[2], Phuoc T. Tran[1,3], Mouen A. Khashab[4],

Lominska *et al. Radiation Oncology* 2012, 7:74
http://www.ro-journal.com/content/7/1/74

RADIATION ONCOLOGY

RESEARCH Open Access

Stereotactic body radiation therapy for reirradiation of localized adenocarcinoma of the pancreas

Chris E Lominska[1*], Keith Unger[2], Nadim M Nasr[3], Nadim Haddad[4] and Greg Gagnon[2]

Although limited treatment options exist for isolated local recurrent PCA after CRT, re-irradiation with SBRT appears to be a safe and reasonable option in well selected cases.

Be careful !!

- **GTV=CTV + 0-5 mm for PTV**
- **Organ motion management**
- **IGRT (CBCT, fiducial markers)**
- **OARs dose constraints**

International Journal of Radiation Oncology biology • physics

www.redjournal.org

Clinical Investigation: Gastrointestinal Cancer

Predictor of Severe Gastroduodenal Toxicity After Stereotactic Body Radiotherapy for Abdominopelvic Malignancies

Int J Radiation Oncol Biol Phys, Vol. 84, No. 4, pp. e469–e474, 2012

Sun Hyun Bae, MD,* Mi-Sook Kim, MD, PhD,* Chul Koo Cho, MD, PhD,*

Table 4 Severe GDT, (≥grade 3) and dose constraints in published studies and recommendations

Study	No. of patients	Origin	RT dose Gy/fx	Dose volume constraints	Severe GDT
Hoyer et al (14)	22	Pancreas cancer	45/3	Not discussed	5 (23%)
Kavanagh et al (15)	36	Limited metastasis	36-60/3	Stomach Maximum ≤30 Gy	No
Rusthoven et al (16)	47	Liver metastasis	60/3	Stomach and duodenum Maximum ≤30 Gy	No
Kopek et al (17)	27	Cholangio carcinoma	45/3	Dose to duodenum as low as possible	7 (26%)
Timmerman RD (13)		Suggested		Stomach Maximum≤24 Gy Duodenum Maximum≤24 Gy	
Current study		Suggested		Stomach and duodenum D_{max} ≤35 Gy	5%

Table 4. Summary of re-irradiation (re-RT) of esophagus after primary definitive (concurrent chemo-) radiotherapy

Author	No.	Re-RT interval[a] (mo)	Treatment at re-RT	Total dose of RT[a] (Gy)		CTx with re-RT, no. (%)	Toxicity over grade 3 non-hematologic (no.)	Survival time after re-RT[a] (mo)
				Initial RT	Re-RT			
Yamaguchi et al. [11]	C						EH (1),	Cu: 18.6 Pa: 6.5
Nonoshita et al. [12]							city	30.0 (14.4-35.8)
Teli et al. [13]							no TEF	7.9
Harms et al. [10]	16	15 (4-37)	PDR	50 (46-60)	15-20	NA	TEF (2), FAB (1), ES (1)	8 (4-19)

CTx, concurrent chemotherapy; Cu, curative group; Pa, palliative group; NA, not assessed; HDRB, high-dose-rate brachytherapy; PDR, pulsed dose rate brachytherapy; EP, esophageal perforation; ES, esophageal stricture; EH, esophageal hemorrhage; PE, pericardial effusion; TEF, tracheoesophageal fistula; FAB, fatal arterial bleeding.

In conclusion, because of the small number of patients, it is difficult to generalize prognostic factors related to severe toxicity with re-RT. Re-RT of recurrent esophageal cancer after primary radiotherapy can cause severe toxicity.

Bonomo et al. 2013	26 pts, 32 abdomino-pelvic LN mts	retrospective	LINAC with dynamic arc	ellaneous ommon: ic, and
Alongi et al. 2012	25 pts, 28 abdom	retro	ams	ellaneous
Corvò et		ive	IG-IMRT (helical Tomotherapy ™ Hi-ART)	miscellaneous, (most common pancreas and colon)

RE-RT SBRT: really poor !!

OARs Dose constraints SBRT: be careful !!

80-90%

Mean follow-up < 2 years

Table 3.3 Summary of radiation threshold dose constraints for stereotactic and hypofractionated schedules publishe in the literature

Organ	Max critical volume	One fraction (Gy)	Three fractions (Gy)	Five fractions (Gy)	End point grade 3
Brain	100 %			20	Necrosis
Brain stem	<0.5 cc	10	18 (6 Gy/fx	23 (4.6 Gy/fx	Neuropathy
Spinal cord	< 1.2 cc	7	12.3(4.1 Gy/fx)	14.5 (2.9 Gy/fx	Myelopathy
Optic nerve	0.2 cc	08-ott	15	20	Neuropathy
Cochlea		10	17	23	Hearing loss
Larynx	4 cc	10		20	
Brachial plexus	3 cc	14	22.05	30	Neuropathy
Bronchus	< 4 cc	10	15 (5 Gy/fx)	16.5 (3.3 Gy)	
Lung	1,000 cc	07.04	10.5 (4 Gy/fx)	13.5 (2.7 Gy/fx)	Pneumonitis
Heart	< 15 cc	16	24 (8 Gy/fx)	32 (6 Gy/fx)	Pericarditis
Esophagus	< 5 cc	11.09	17	20	Stenosis
Rib	< 1 cc	22	28	35	Fracture
Stomach	< 10 cc	11	16.5 (5 Gy/fx)	18 (3.6 Gy/fx)	Ulceration
Duodenum	< 10 cc	9	11.04	12.05	Stenosis
Small bowel	< 5 cc	11.09	17.7 (5.9Gy/fx)	19.05	Stenosis
Colon/rectum	< 20 cc	14.03	16.8 (5.6 Gy/fx)	18.3 (3.6 Gy/fx)	Colitis Proctitis
Liver	< 700 cc	9	19 (6.4 Gy/fx)	21 (4.2 Gy/fx)	Liver function
Kidney	< 200 cc	08.04	16 (4 Gy/fx)	17.5 (3.5 Gy)	Renal function
Bladder	< 15 cc	11.04	16.8 (5.6 Gy)	18 (3.6 Gy/fx)	Cystitis
Penile bulb	< 3 cc	14	21.9 (7.3 Gy)	30 (6 Gy/fx)	Erectile dysfunction
Skin	< 10 cc	23	30 (10 Gy/fx)	36.5(7.3 Gy)	Ulceration

Table II. The characteristics of the patients with recurrent rectal cancer, and the description of low-dose ultrafractionated radiotherapy, anti-tumor response, and toxicity.

Patient, sex, age, and tumor type	Prior chemotherapy regimens	Prior surgery	Prior radiotherapy	Interval to LDUF RT	LDUF RT	Symptom and its grade before LDUF RT	Clinical response after LDUF RT	Radiological response and its duration after LDUF RT	Toxicity	
									Acute	Late
#6 F, 43 years, rectal cancer, T3N0M0	3	2	28 ×2.0 Gy Total 56 Gy	2 years	60 × 0.66 Gy Total 39.6 Gy	Tumor pain (4) Secretion from the natal cleft fistula (4)	Tumor pain (1) Secretion from the natal cleft fistula (2)	PR for 9 months, then local progression	No	No
#7 M, 60 years, rectal cancer, T2N0M0	2	2	28 ×1.8 Gy Total 50.4 Gy	1 year	83 × 0.5 Gy Total 41.5 Gy	Tumor pain (4) Secretion from the natal cleft fistula (4)	Tumor pain (2) Secretion from the natal cleft fistula (2)	SD for 3 months, then local progression and distant metastases	No	NR
#8 M, 62 years, rectal cancer, T4N1M0	3	1	25 ×2.0 Gy Total 50 Gy	4 years	99 × 0.5 Gy Total 49.5 Gy	Rectal discharge (3)	Rectal discharge (1)	SD for 12 months, then local progression and distant metastases	No	No

LDUF RT = low-dose ultrafractionated radiotherapy; PR = partial response; SD = stable disease.
NR = no referrals.

Conclusions

- RE-RT in GI tumor: poor data; pz selection
- RE-RT in Rectal cancer: iperfx/small volumes
- Radiobiologic principles: +++
- SBRT: a great potential but…

  … great attention to:

  - Clinical volumes
  - OARs dose constraints for ipofx Re-RT
  - IGRT for organ motion & check
  - Method & Uniformity
  - Clinical multicentric studies

- Low-dose Re-RT: palliative setting