TRATTAMENTO NON CHIRURGICO DELLE OLIGOMETASTASI

Fegato

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CATANZARO

Dimensioni del problema

2a causa di morte negli USA

- Circa il 50% dei pazienti affetti da cancro del colon-retto in stadio III e circa il 20% in stadio II è destinato a sviluppare metastasi epatiche nel corso della malattia.
- La sopravvivenza a 5 anni dopo chirurgia delle metastasi epatiche varia fra il 26 e il 49%.
- Dopo una prima resezione chirurgica, il 60% dei pazienti andrà incontro a nuove metastasi
- Nel 15% sincrona, nel 15% metacrona (prossimi 5 anni)
- Resacabili all'inizio nel **1/4- 1/5 dei pazienti**
- ~10-20% dei pazienti rimanenti può diventare resecabile

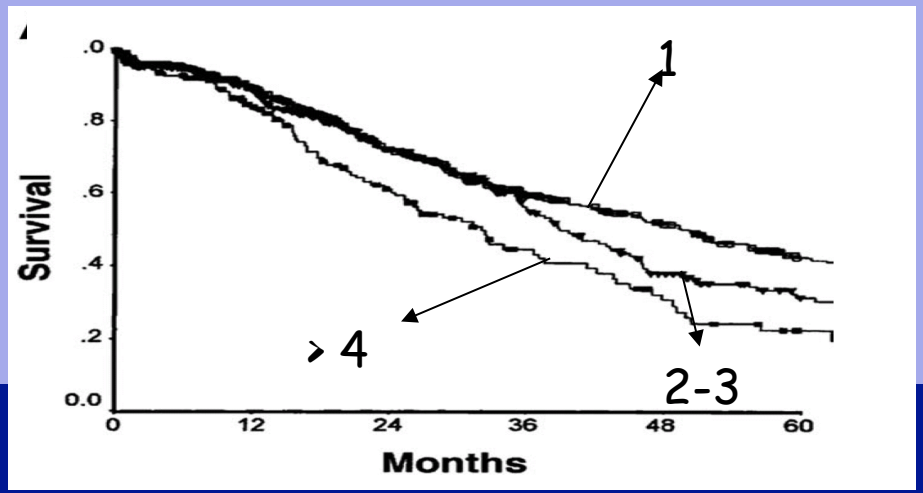
Unica metastasi in quasi la ½ dei pazienti

Engstrom PF, et al. NCCN Clinical Practice Guidelines in Oncology: colon cancer. J Natl Compr Canc Netw 2009

Oligometastasi

< 5 noduli, < 5 cm totali e limitate ad 1 organo

(Rubin P et al Semin Radiat Oncol. 2006 Apr;16(2):120-30)



*Yin FF et Semin Radiat Oncol. 2006 Apr;16(2):85-101

Stadiazione

- Metastasi: Mic-M4
- Markers: S0- S3
- Sintomi: A - B
- Karnofsky: H0-H5

Stadiazione: M

- **Mic:** cellule isolate in circolo, < 0.1 mm
- **M1mic:** micrometastasi, > 0.2 mm fino a 2 mm
- **M1:** singola metastasi, in singolo organo
- M2: oligometastasi, limitate ad 1 organo

(< 5 metastasi < 5 cm)

- **M3:** multiple metastasi , limitate ad 1 organo

(> 5 metastasi > 5 cm, più di 1 polmone)

- **M4:** multiple metastasi, in più organi

Karnofsky scale

- **H0:** normale attività, asintomatico
- **H1:** sintomatico, ma ambulatoriale
- **H2:** sintomatico e costretto a letto < 50% del tempo
- **H3:** sintomatico,a letto > 50% del tempo, non allettato
- **H4:** 100% allettato

Marcatori sierici:

- **S0:** non rilevabile
- **S1:** bassi livelli
- **S2:** livello intermedio
- **S3:** alto livello

Segni Sistemici:

A: *non segni sistemici*

- < 5% perdita peso
- lievi anormalità laboratoristiche

B: *segni sistemici*

- 100% perdita peso
- febbre ndd
- cachessia
- anormalità laboratoristiche

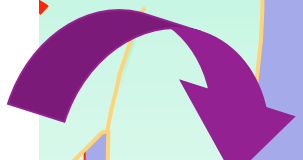
Rubin P et al Semin Radiat Oncol. 2006 Apr;16(2):120-30

Caso clinico

Uomo di anni 69
Neoplasia prostatica
TC di Centraggio

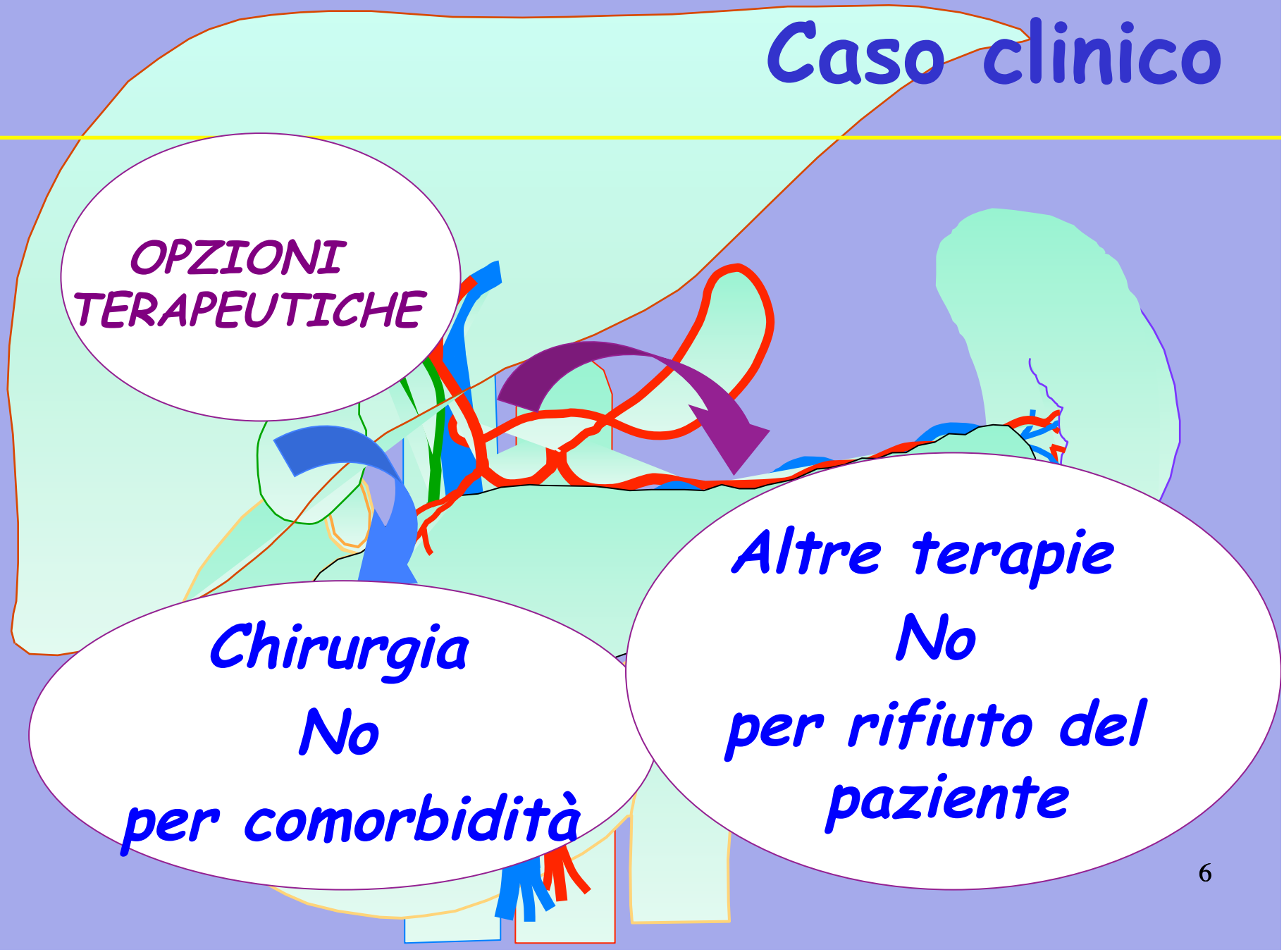
Durante la TC di Centraggio riferisce dolore in ipocondrio di destra. TC addome superiore: evidenziata una neoformazione IV segmento subglissoniana

TC total body con mdc
FDG-PET



- *OLIGOMETASTASI*

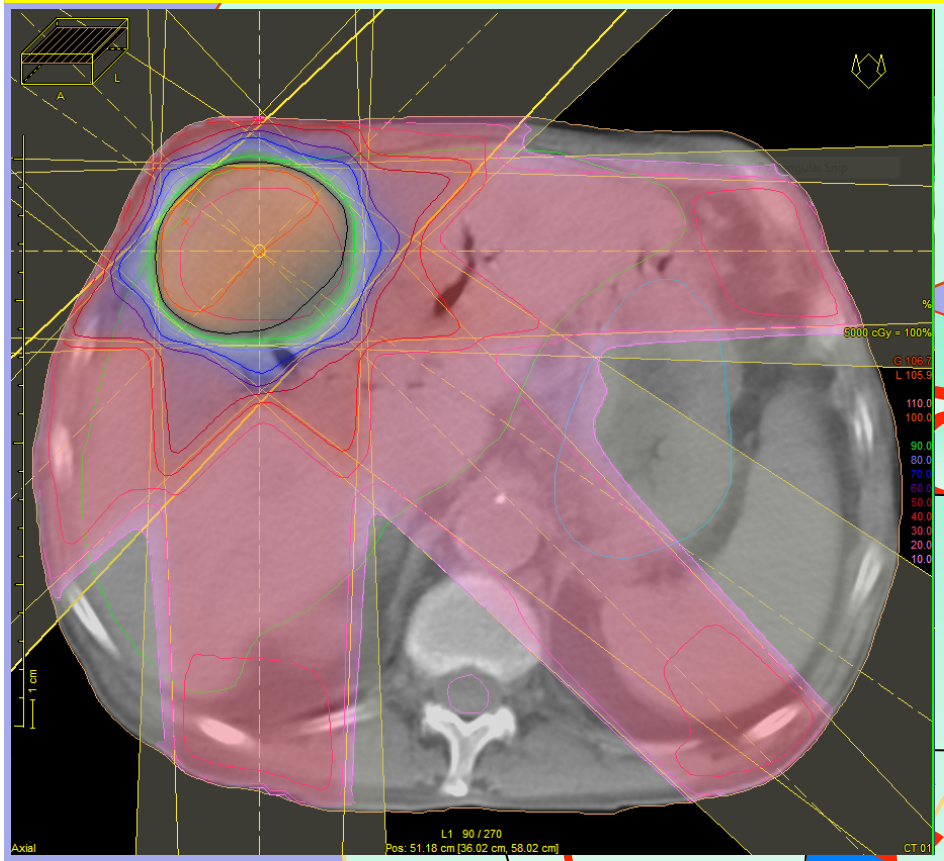
Caso clinico

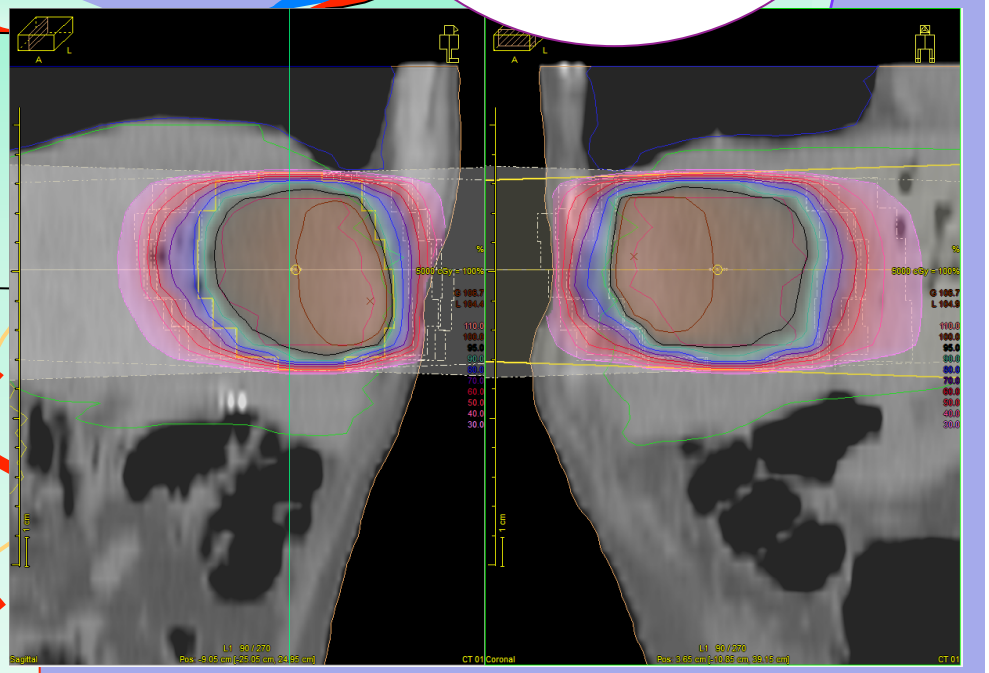


Caso clinico

Curve di isodose

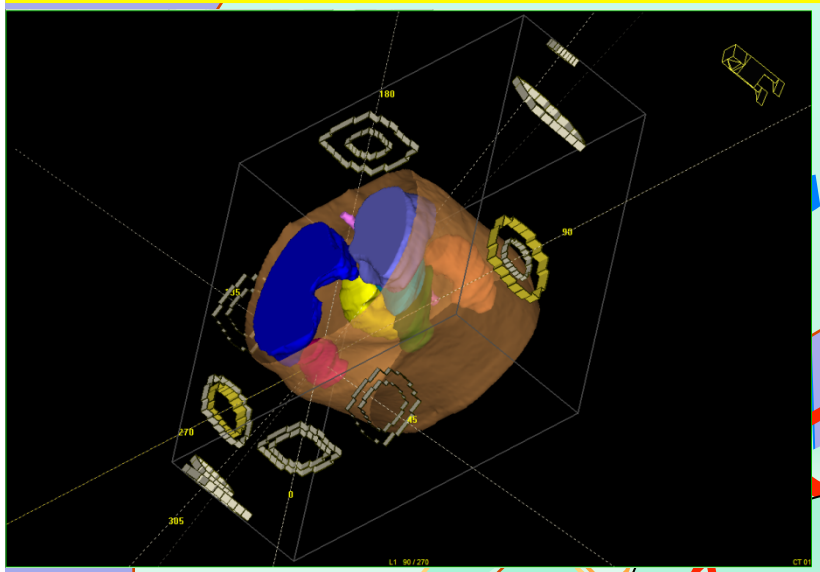
Dose totale
5000 cGy
Dose a fraz.
125 cGy
b.i.d

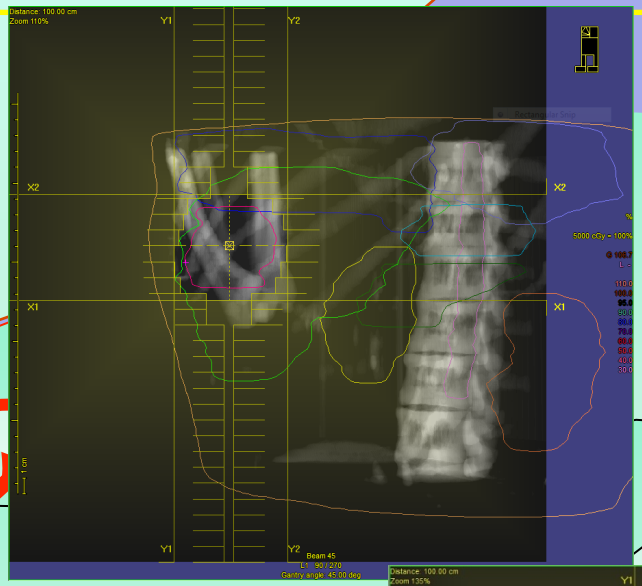


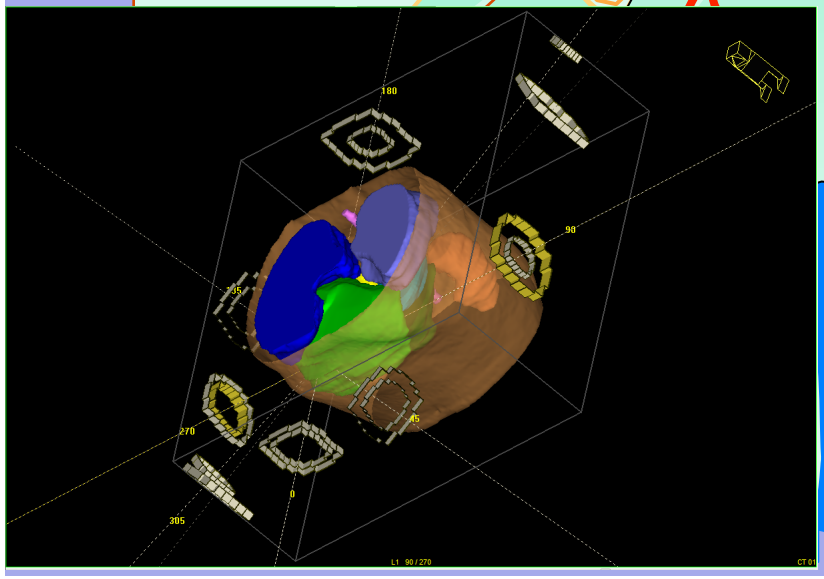


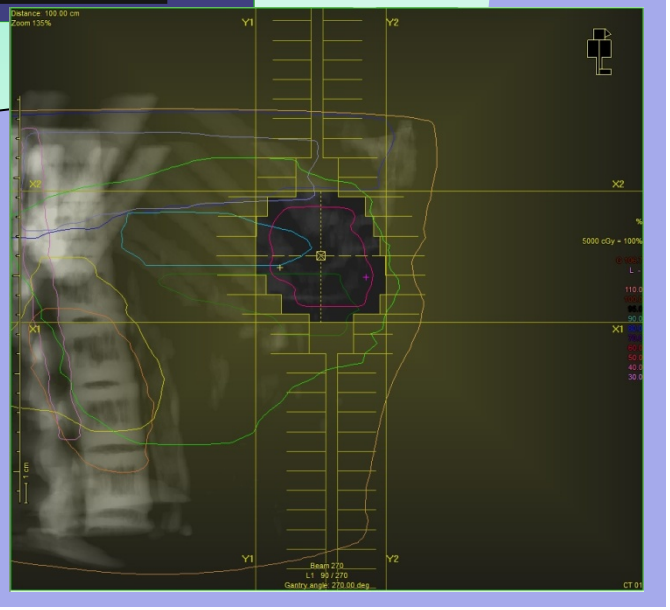
Caso clinico

BEV e DRR





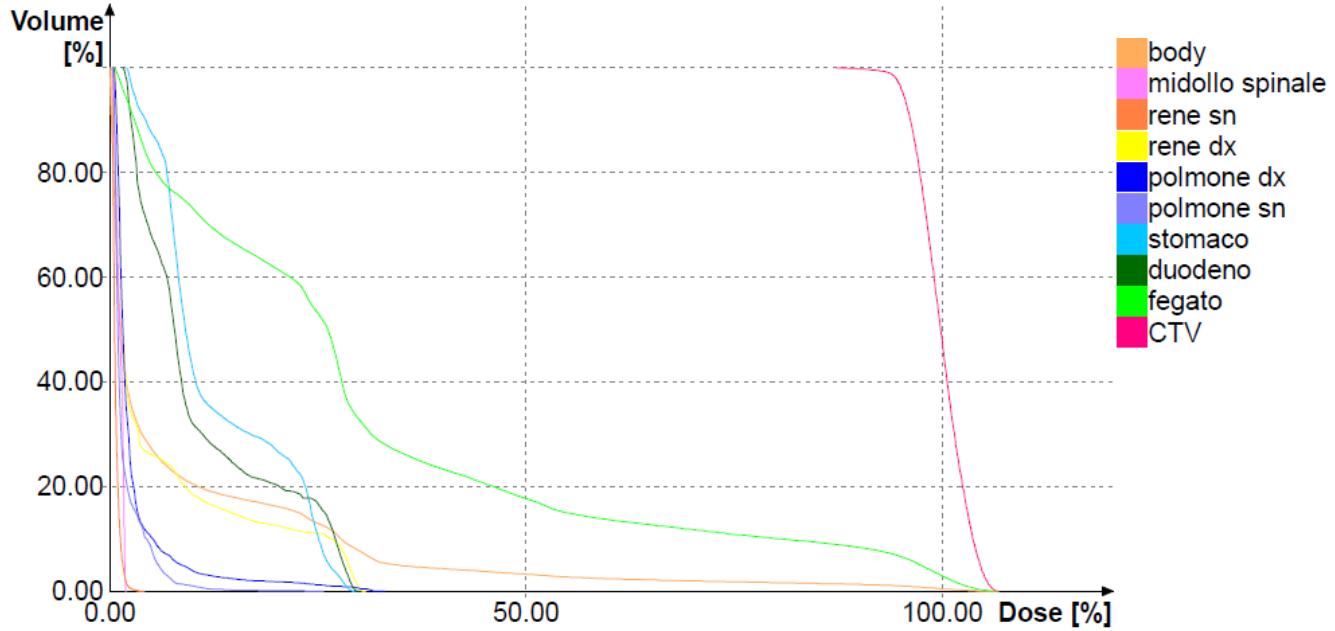




Caso clinico

DVH

Patient name	
Patient ID	
Case	
Plan	
Current plan object	
Treatment position	
Last saved	24-Jun-2013 13:33:33
Approval status	APPROVED
Reviewed	24-Jun-2013 13:33:30
Reviewer name	sergio
Printed	24-Jun-2013 13:35:34
Time zone	W. Europe Standard Time (UTC+1:00), W. Europe Daylight Time



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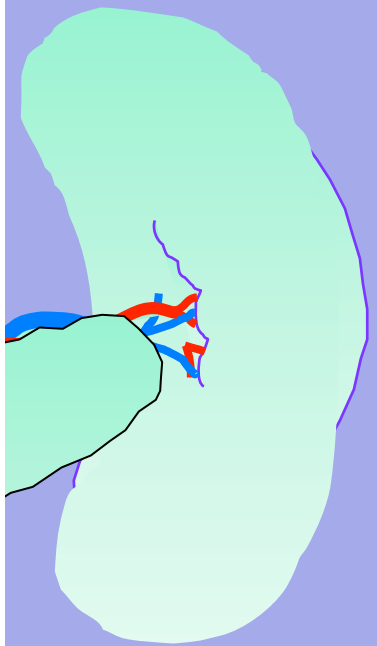
Printed 24-Jun-2013 13:35:34
Time zone W. Europe Standard Time (UTC+1:00), W. Europe Daylight Time

Dose Statistics and Volume Information

Name	Type	Min [%]	Max [%]	Median [%]	Average [%]	Std. Dev. [%]	Calc.pts	Dose Volume [ccm]
body	ROI	0.00	106.69	1.28	8.38	16.60	439305	13462.145
midollo spinale	ROI	0.46	1.94	1.25	1.23	0.46	823	26.122
rene sn	ROI	0.27	3.46	0.60	0.72	0.42	6142	192.352
rene dx	ROI	0.67	30.53	1.62	6.02	8.96	7707	240.405
polmone dx	ROI	0.51	31.93	1.50	2.61	4.08	22537	657.258
polmone sn	ROI	0.43	23.99	0.95	1.68	2.05	17487	520.907
stomaco	ROI	2.11	29.37	9.08	12.65	7.97	4733	136.608
duodeno	ROI	1.71	29.70	7.87	10.91	8.80	3369	96.890
fegato	ROI	0.67	106.69	26.34	30.93	27.64	61970	1926.955
CTV	ROI	89.69	106.69	99.84	100.00	2.87	2931	88.940



Caso clinico

Parametri fisici-dosimetrici

MLD 1550 cGy

(QUANTEC mean liver dose< 32 cGy)

20% del volume <250 cGy

28% del volume <500 cGy

Isodose del 90 copre il 99.8% del target

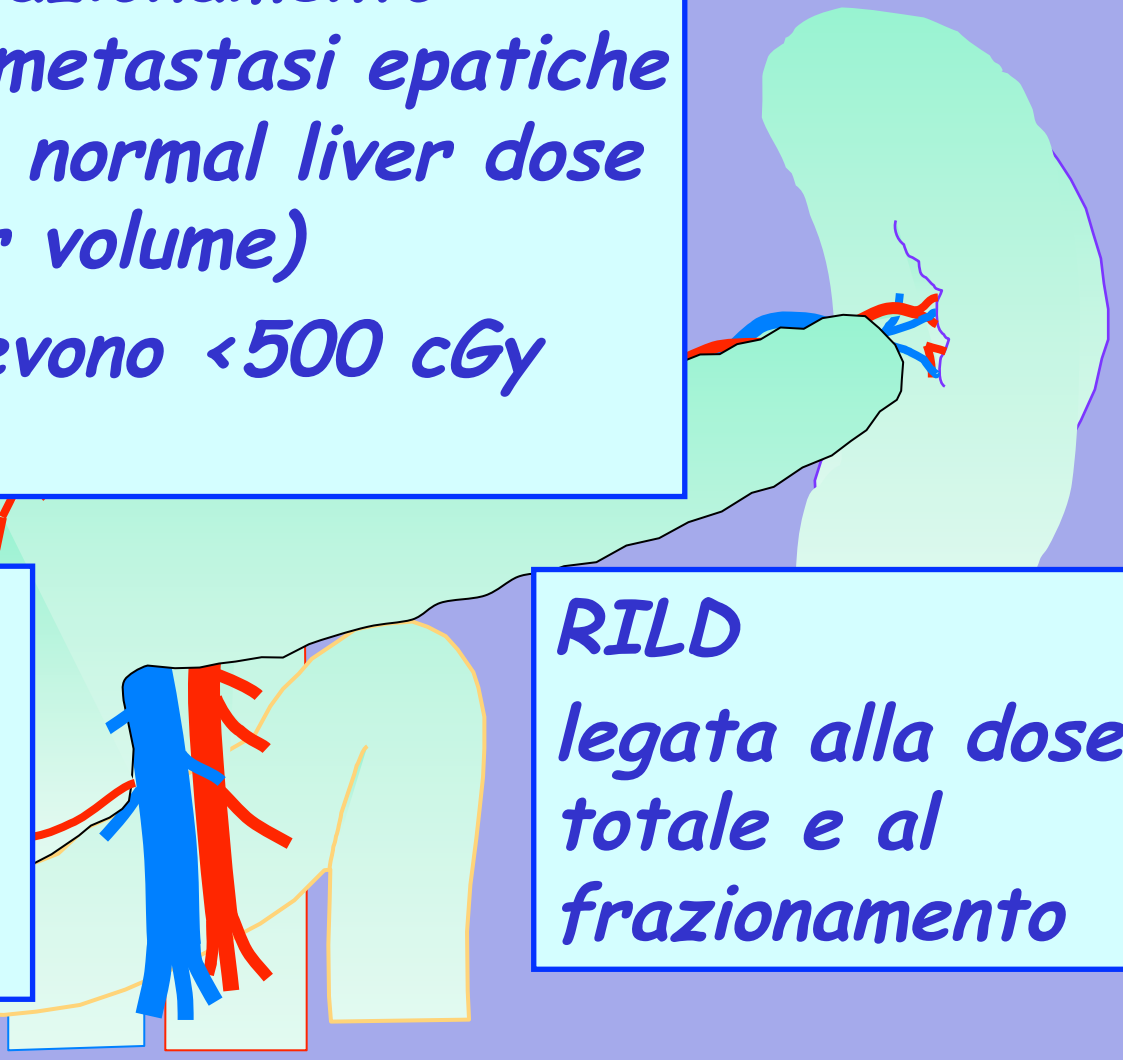
Isodose del 95 copre il 96% del target

Isodose del 98 copre il 80% del target

Caso clinico

RILD del <5%: frazionamento standard per le metastasi epatiche <3200 cGy, mean normal liver dose (liver minus tumor volume)

> 700 cc che ricevono <500 cGy



Danno molto tipico alle vene centrali del lobulo

RILD

legata alla dose totale e al frazionamento

Caso clinico

Pianificazione

- CTV: margini (0.5-1 cm)
- PTV : margini 0.6-1 cm sul piano trasverso e 1-1.5 cm sul piano longitudinale
- Intrafraction motion:
  - normale respirazione 10-25 mm
  - respirazione profonda: 37-55 mm

Importanza del Posizionamento Immobilizzazione

Conformal RT

What is the expected outcome after CRT for liver metastases?.

Le percentuali di risposta: 50-60%, ma solo il 25 % 1 anno senza progressione

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0360-3016/$ - see front matter

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CRITICAL REVIEW

RADIOTHERAPY FOR LIVER METASTASES: A REVIEW OF EVIDENCE

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Quantec

Int. J. Radiation Oncology Biol. Phys., Vol. 76, No. 3, Supplement, pp. S94–S100, 2010

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QUANTEC: ORGAN-SPECIFIC PAPER **Abdomen: Liver**

RADIATION-ASSOCIATED LIVER INJURY

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The liver is a critically important organ that has numerous functions including the production of bile, metabolism of ingested nutrients, elimination of many waste products, glycogen storage, and plasma protein synthesis. The liver is often incidentally irradiated during radiation therapy (RT) for tumors in the upper- abdomen, right lower lung, distal esophagus, or during whole abdomen or whole body RT. This article describes the endpoints, time-course, and dose-volume effect of radiation on the liver. © 2010 Elsevier Inc.

Liver, Normal tissue toxicity, Radiation-induced liver disease.

Table 2. Series of fractionated partial liver irradiation and rates of RILD

Study group	*n*	Diagnosis	Baseline Child-Pugh score	Prescription dose fractionation	Crude percent RILD	Mean normal liver dose in patients with vs. without RILD	Factors associated with RILD
Michigan (8, 23)	203*	PLC + LMC	203 A	1.5 Gy twice daily	9.4% (19/203)	37 Gy vs. 31.3 Gy	PLC vs. LMC mean liver dose
Taipei (20)	89†	HCC	68 A 21 B	1.8–3.0 Gy	19% (17/89)	23 Gy vs. 19 Gy	HBV, liver cirrhosis
Shanghai (3, 18)	109†	PLC	93 A 16 B	4–6 Gy	15.6% (17/109)	24.9 Gy vs. 19.9 Gy	Liver cirrhosis
Guangdong (20)	94**	HCC	43 A 51 B	4–8 Gy	17% (16/94) Note: 4 fatal	Not stated	Liver cirrhosis
S. Korea (Seong, Park) (21)	158†	HCC	117 A 41 B	1.8 Gy	7% (11/158)	Not stated	Dose
S. Korea (Kim) (4)	105†	HCC	85 A 20 B	2.0 Gy	12.3% (13/105)	25.4 Gy vs. 19.1 Gy	Total liver volume receiving 30 Gy or more above 60%

Abbreviations: HBV = hepatitis B viral infection; HCC = hepatocellular carcinoma; PLC = primary liver cancer; LMC = liver metastatic disease; RILD = radiation-induced liver damage.

* Patients also received FUdR or BUdR; in this series the mean normal liver dose was calculated as corrected for 1.5 Gy twice-daily equivalent dose, and the comparison of patients with vs. without RILD refers to the median value of mean normal liver dose, whereas for other series the comparison is between the average (mean) of mean normal liver dose in each group.

† At least 77% of patients in these series also received transarterial chemoembolization (TACE).

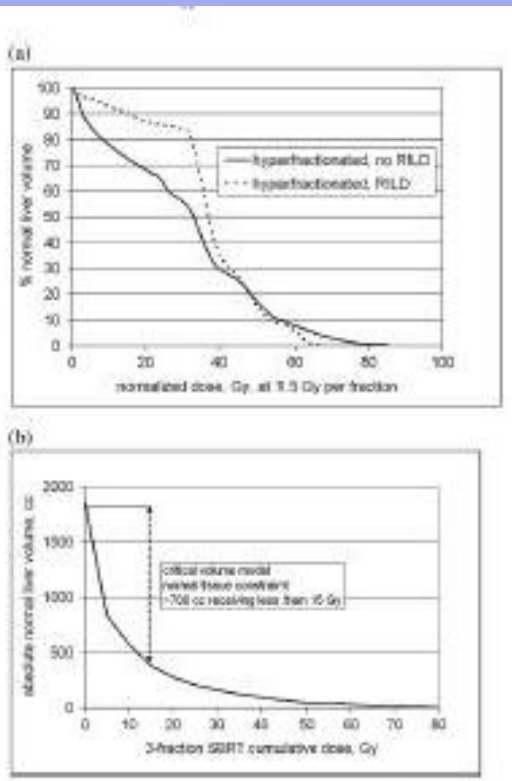

Fig. 3. Characteristic normal liver (minus gross tumor volume) DVHs for low (a) or high (b) dose per fraction. (a) Mean normal liver DVHs from the University of Michigan for 204 patients who did or did not experience radiation-induced liver disease (RILD). (b) Mean normal liver dose–volume histogram from the University of Colorado SBRT Phase I trial with no RILD observed. See text for additional details.