

C089

ABBIAMO FEGATO? INDAGINE CONOSCITIVA SUL RUOLO DEL RADIOTERAPISTA ONCOLOGO NEL TRATTAMENTO DELLE LESIONI PRIMITIVE E SECONDARIE EPATICHE

F. Dionisi, A. Guarneri, V. Dell'Acqua, MC. Leonardi, R. Niespolo, per conto del Gruppo di studio AIRO per i Tumori Gastrointestinali (AIRO GI)

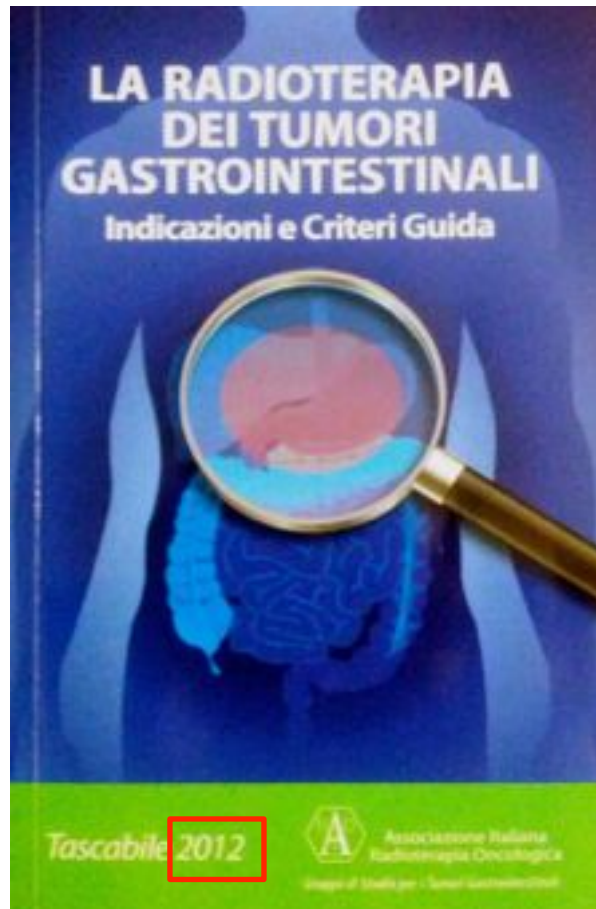
UO Protonterapia, Dipartimento Oncologico, APSS, Trento



INDICE

- Background
- Presentazione survey
- Risultati
- Discussione

Background



Nuovi Campi di Sviluppo: Fegato

R. Niespolo (Monza); A. Guarneri (Torino); F. Dionisi (Trento); M.C. Leonardi (Milano); V. Dell'Acqua (Milano)

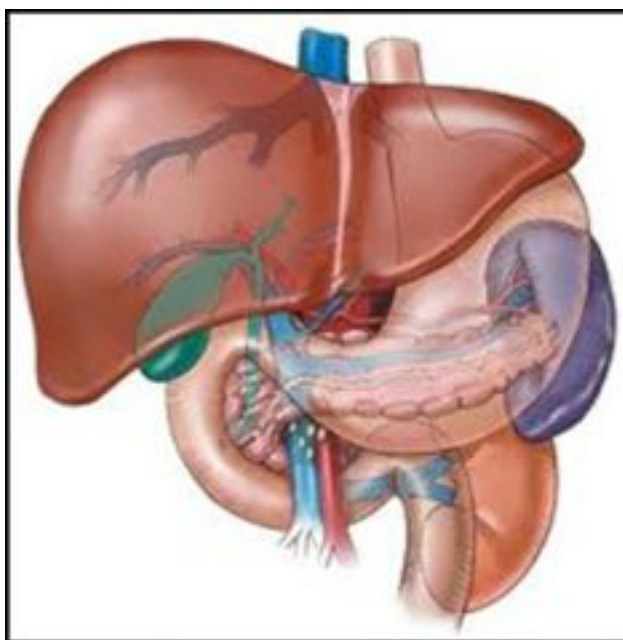
Epatocarcinoma

Metastasi epatiche

CD AGGIORNAMENTO 2014 IN KIT CONGRESSUALE!

Proposta SURVEY

Indagine conoscitiva a cura del gruppo di studio AIRO GI:
“Abbiamo Fegato?”



APPROVATA DAL GRUPPO AIRO GI in data 23.5.14

Presentazione SURVEY

21 DOMANDE SUDDIVISE IN 2 SESSIONI

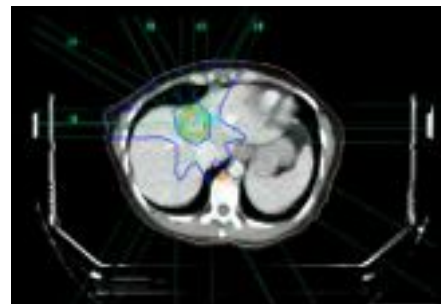
Sessione 1:

PRESA IN CURA-APPROCCIO MULTIDISCIPLINARE



Sessione 2

TRATTAMENTO RADIOTERAPICO



Risultati



Sessione 1:

PRESA IN CURA-APPROCCIO MULTIDISCIPLINARE

DOMANDA N°1



Questionari ricevuti: **36**
20% dei Centri Italiani(SITO AIRO)

16/20 Regioni: **80%**

Aggiornamento a 9-11-14

Risultati



Centri che praticano RT su fegato: **17**

Risultati

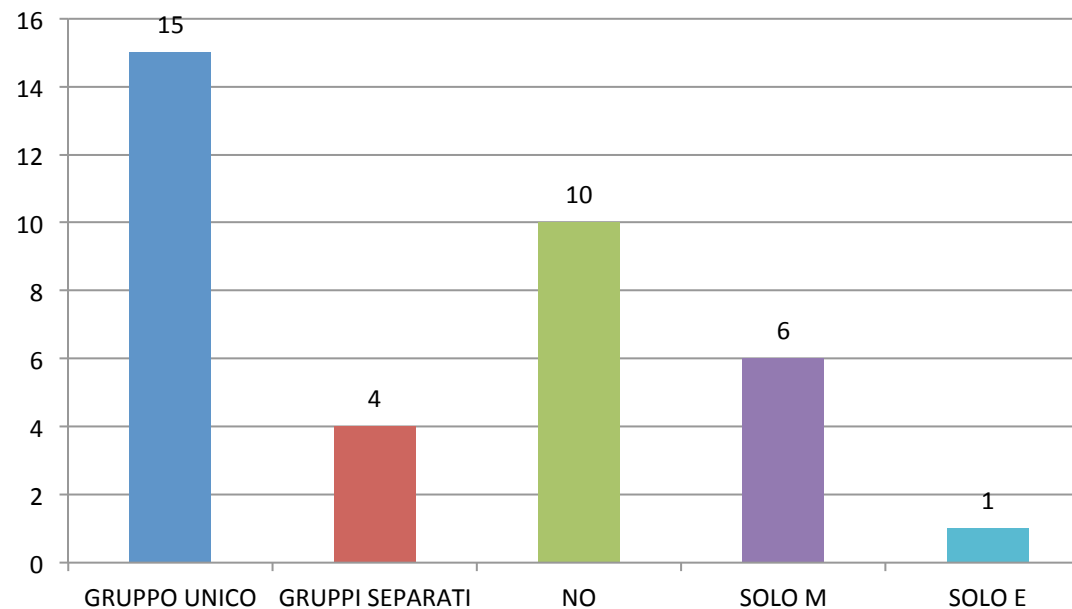


Sessione 1:

PRESA IN CURA-APPROCCIO MULTIDISCIPLINARE

DOMANDA N°3

Esiste presso la tua Struttura Sanitaria un gruppo di lavoro multidisciplinare per il trattamento dei pazienti affetti da epatocarcinoma o neoplasia epatica secondaria ?



Risultati

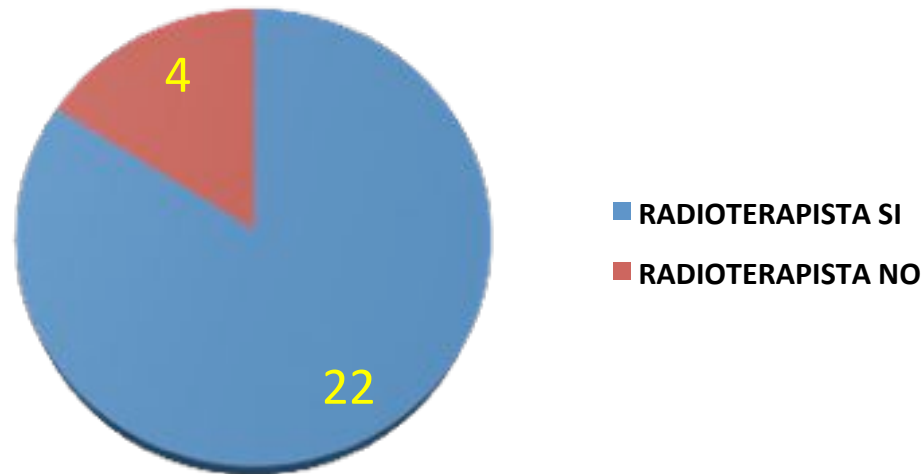


Sessione 1:

PRESA IN CURA-APPROCCIO MULTIDISCIPLINARE

DOMANDA N°4

Componenti del gruppo



Risultati

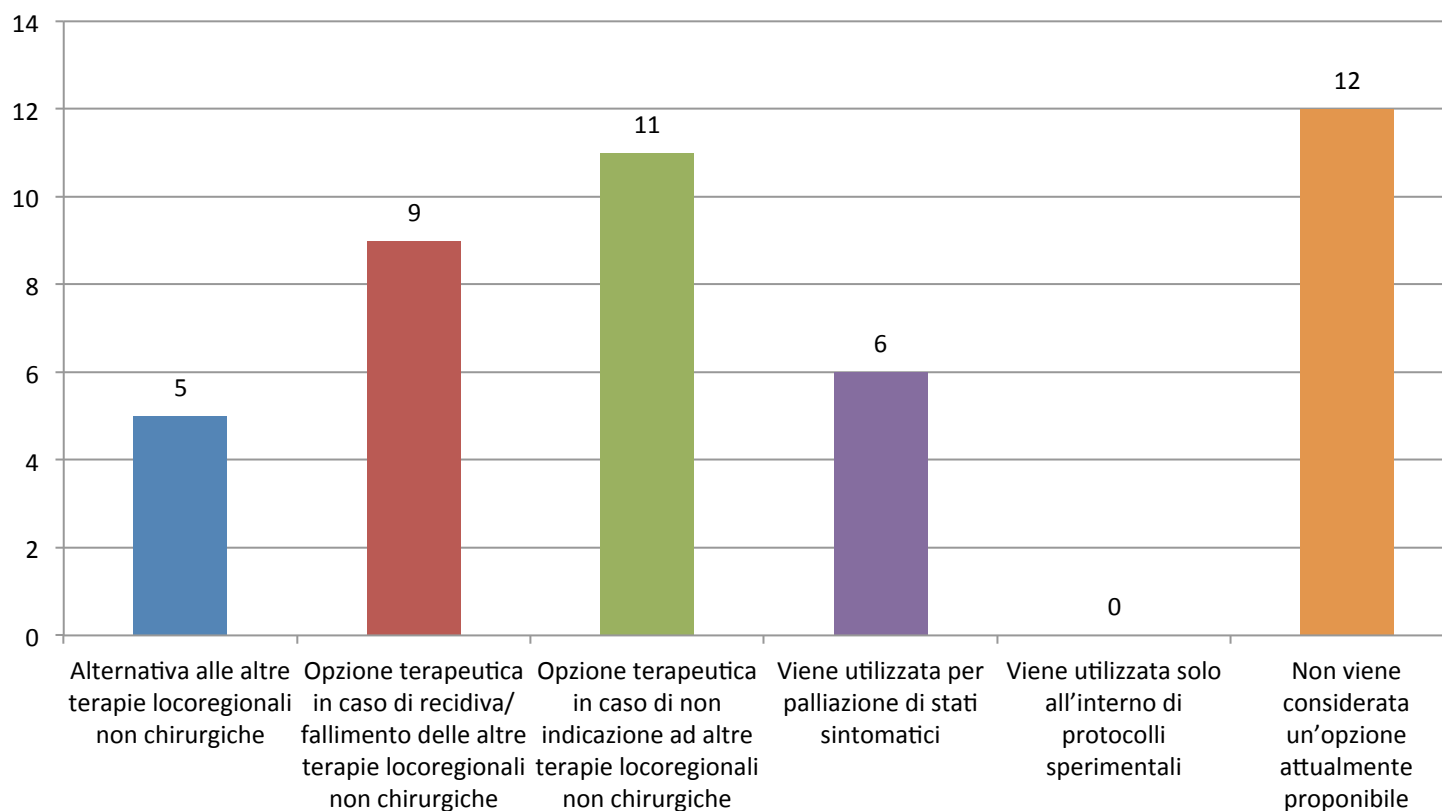


Sessione 1:

PRESA IN CURA-APPROCCIO MULTIDISCIPLINARE

DOMANDA N°5

Come viene valutata l'opzione **Radioterapia** all'interno del gruppo multidisciplinare?
Epatocarcinoma



Risultati

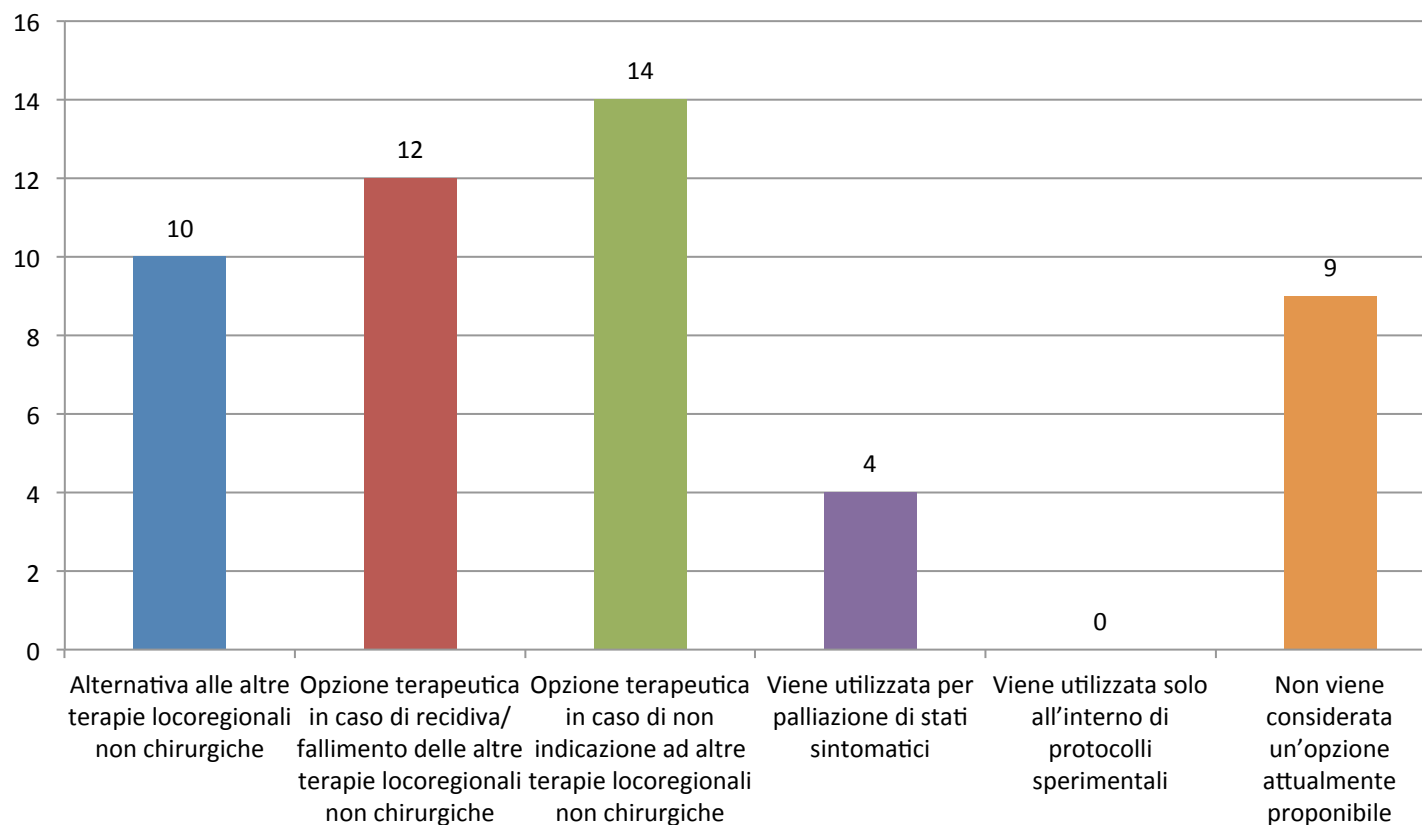


Sessione 1:

PRESA IN CURA-APPROCCIO MULTIDISCIPLINARE

DOMANDA N°5

Come viene valutata l'opzione **Radioterapia** all'interno del gruppo multidisciplinare?
Metastasi epatiche



Risultati

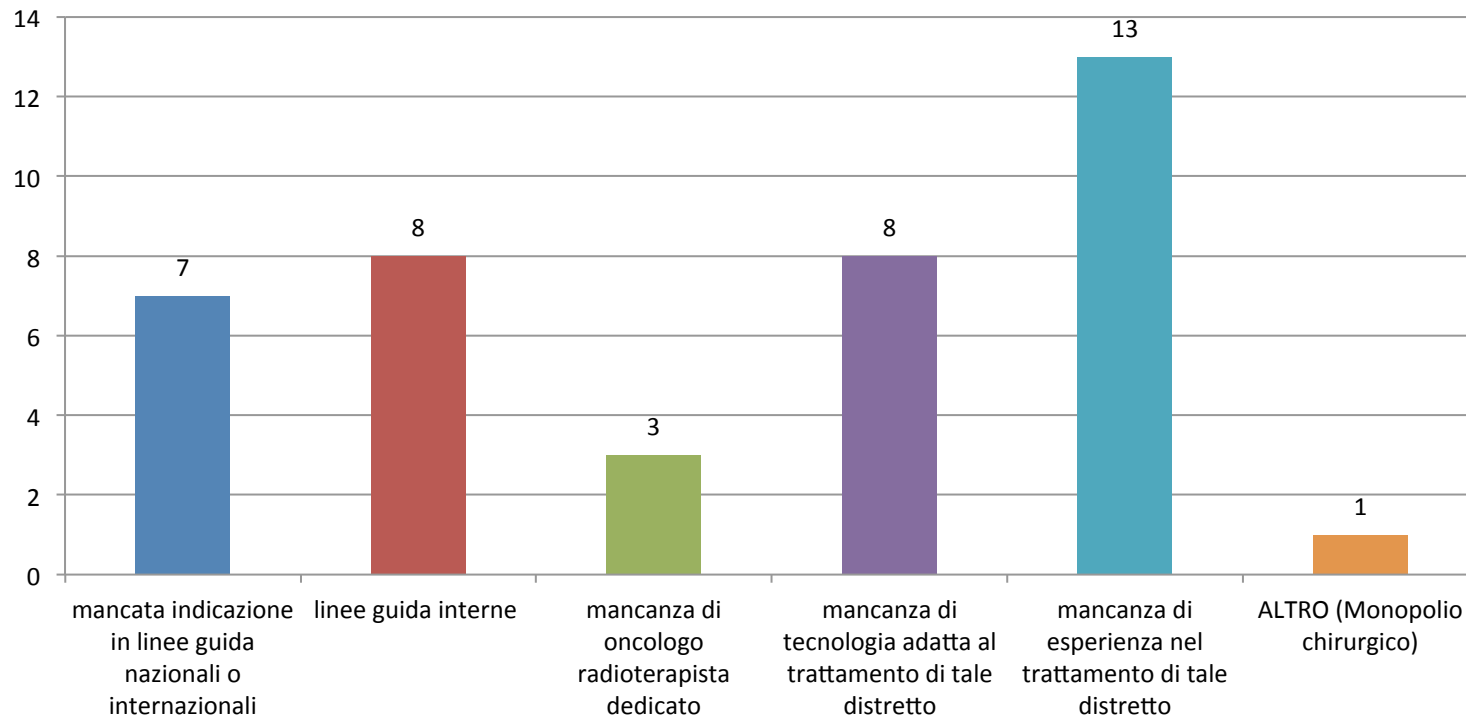


Sessione 1:

PRESA IN CURA-APPROCCIO MULTIDISCIPLINARE

DOMANDA N°6

Principali motivazioni NO RT



Risultati



Sessione 2:

TRATTAMENTO RADIOTERAPICO

DOMANDA N°8

anno di inizio dei trattamenti radioterapici e numero totale di pazienti trattati
EPATOCARCINOMA (14 centri)

INIZIO TRATTAMENTI	PZ trattati
2006	<20
2013	<20
2011	<20
2014	<20
2002	<20
2013	<20
2011	<20
2013	<20
2012	> 50
1995	> 50
2014	inizio valutazione
2013	<20
2006	> 20 ≤ 30
2009	>50

Risultati



Sessione 2:

TRATTAMENTO RADIOTERAPICO

DOMANDA N°8

anno di inizio dei trattamenti radioterapici e numero totale di pazienti trattati

Metastasi epatiche

INIZIO TRATTAMENTI	PZ trattati
2014	<20
2002	$> 30 \leq 50$
2007	$> 20 \leq 30$
2012	<20
2012	<20
2011	$> 20 \leq 30$
2014	<20
2002	> 50
2006	$> 30 \leq 50$
2007	$> 30 \leq 50$
2012	<20
2003	$> 30 \leq 50$
1995	> 50
2014	2
2013	<20
2006	> 50
2009	> 50



Associazione Italiana
Radioterapia Oncologica

Gruppo di Studio per i Tumori Gastrointestinali



Azienda Provinciale
per i Servizi Sanitari
Provincia Autonoma di Trento

Risultati

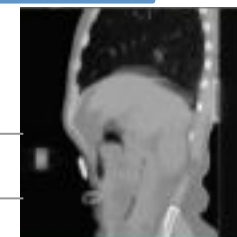
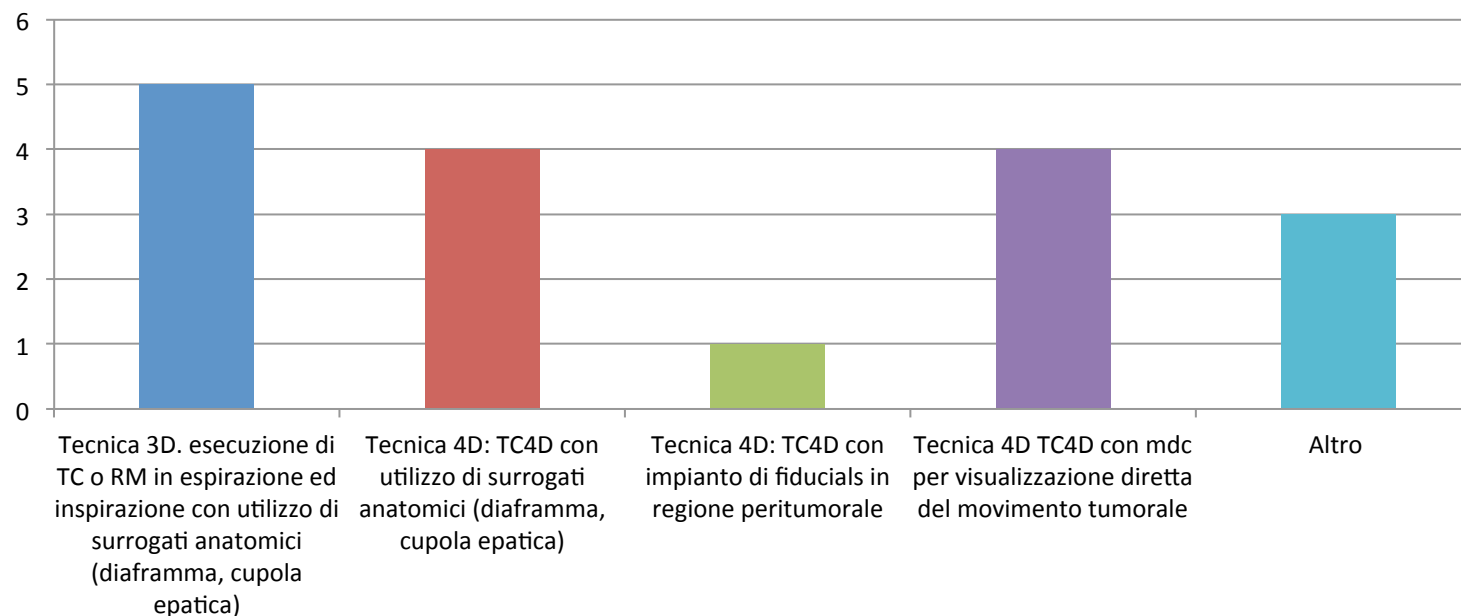


Sessione 2:

TRATTAMENTO RADIOTERAPICO

DOMANDA N°11

Quale metodica di imaging viene tipicamente utilizzata per quantificare il movimento d'organo/tumorale ?



Risultati

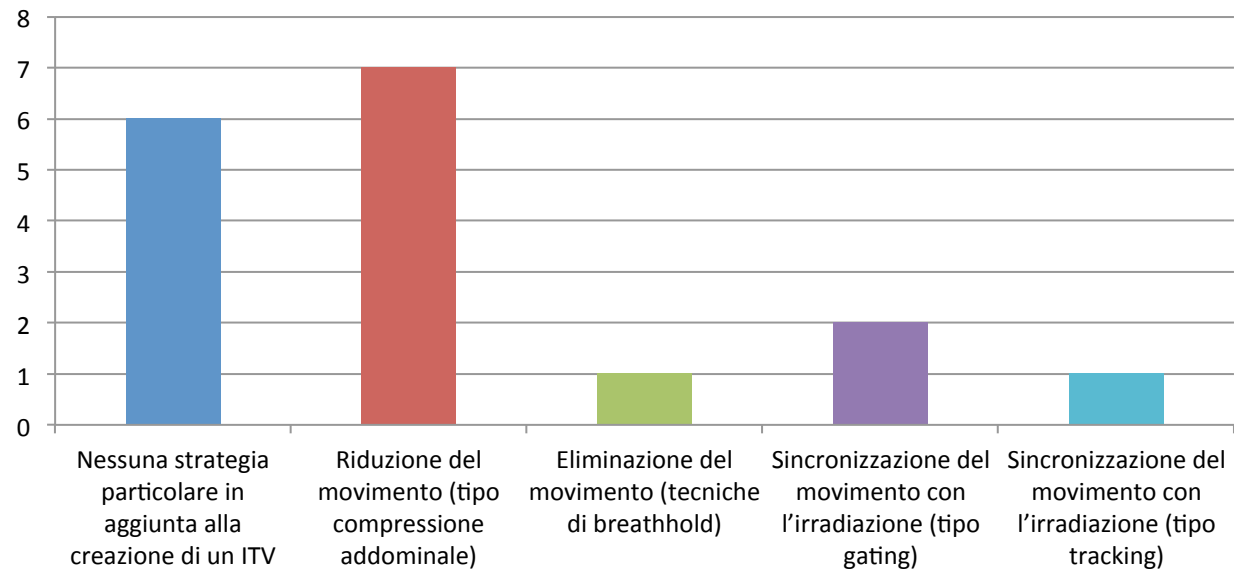


Sessione 2:

TRATTAMENTO RADIOTERAPICO

DOMANDA N°12

Strategie per la gestione del movimento d'organo/tumorale



Risultati

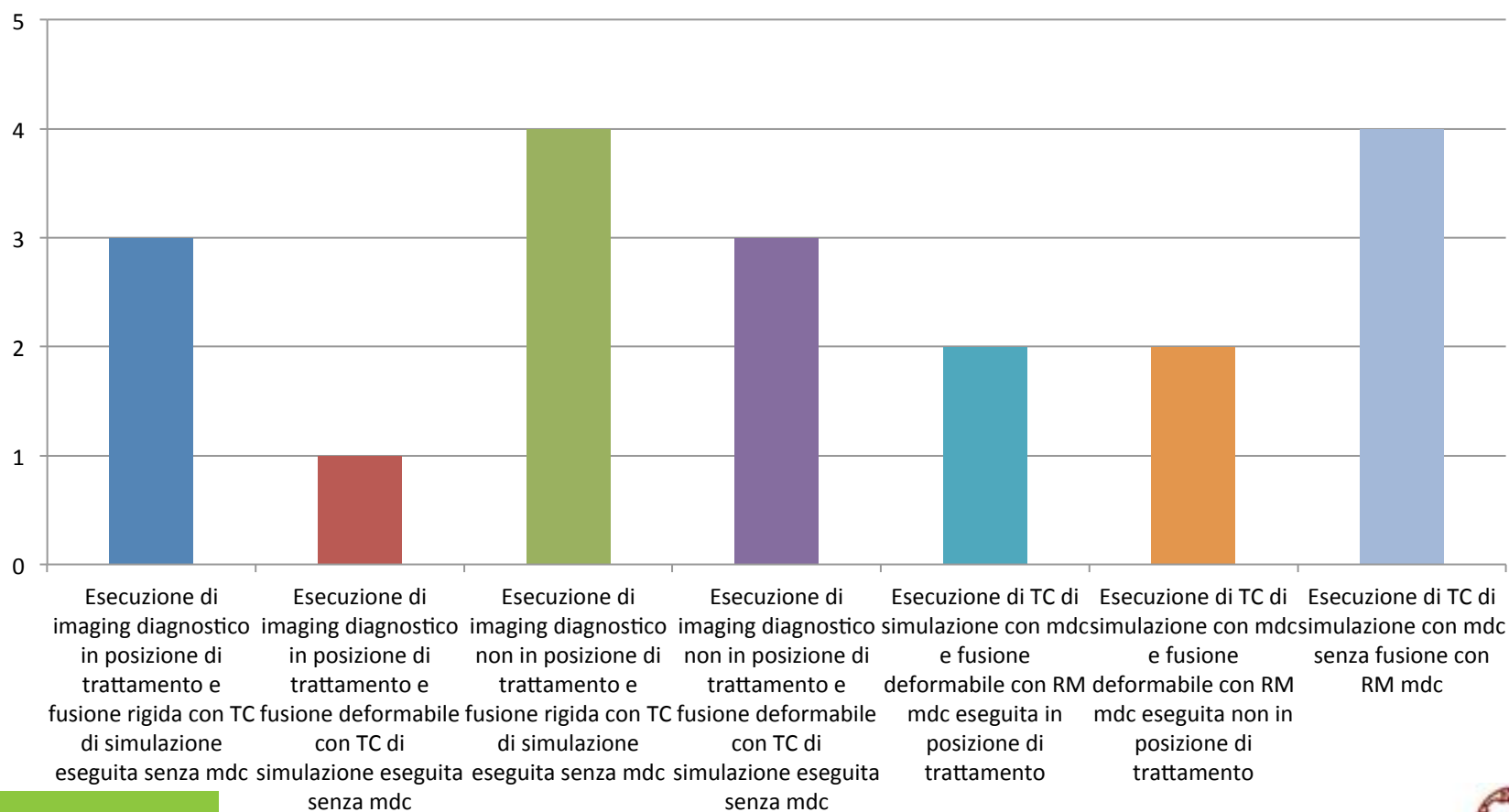


Sessione 2:

TRATTAMENTO RADIOTERAPICO

DOMANDA N°13

Quale workflow viene seguito per la definizione del GTV ?



Risultati

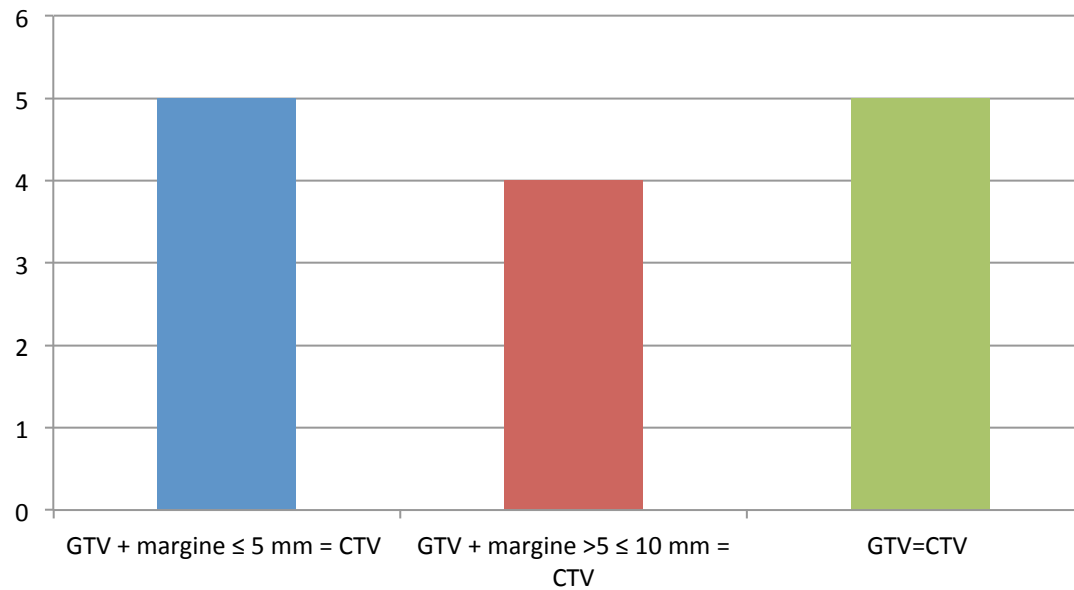


Sessione 2:

TRATTAMENTO RADIOTERAPICO

DOMANDA N°14

**volume clinico di trattamento (CTV)
EPATOCARCINOMA**



Risultati

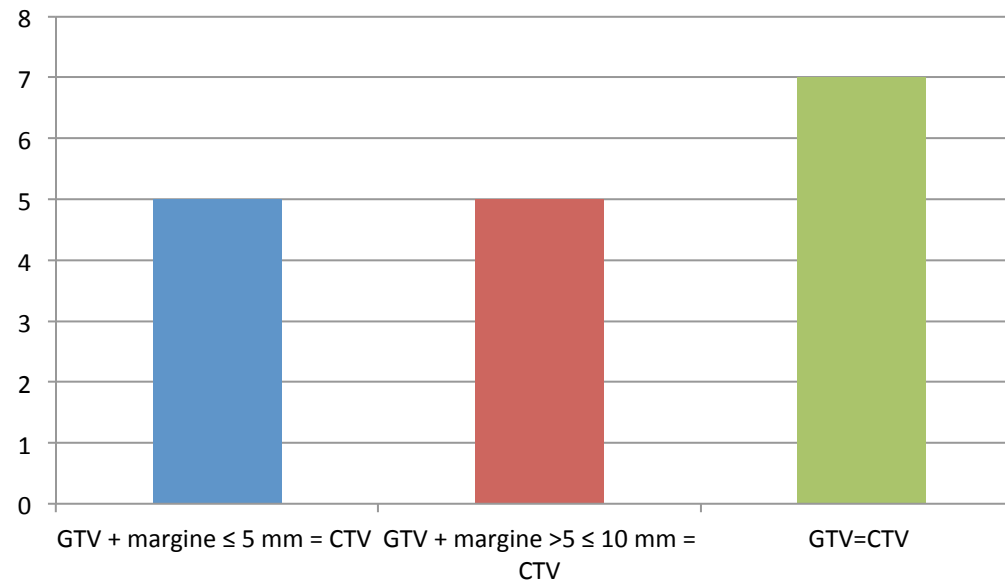


Sessione 2:

TRATTAMENTO RADIOTERAPICO

DOMANDA N°14

**volume clinico di trattamento (CTV)
METASTASI EPATICHE**



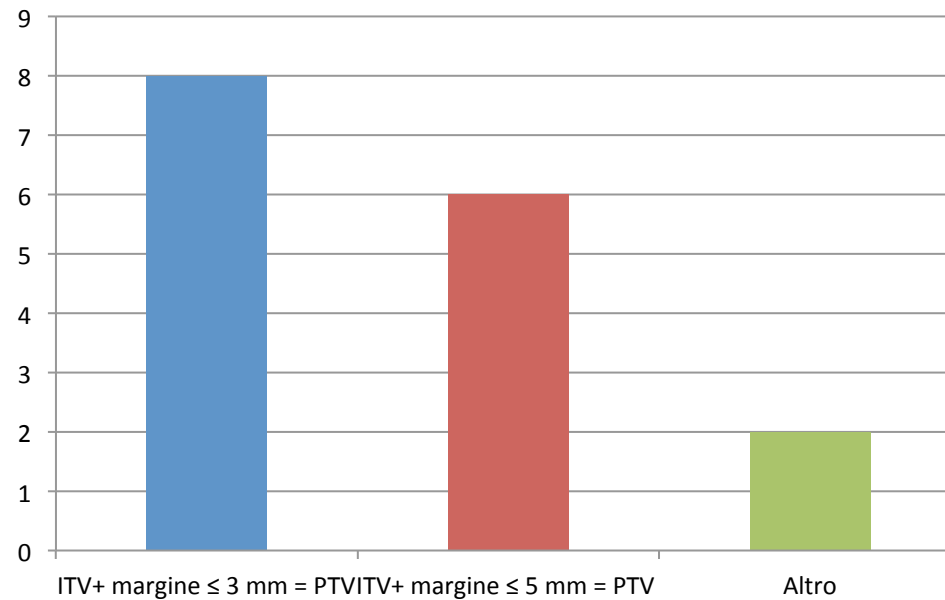
Risultati



Sessione 2:
TRATTAMENTO RADIOTERAPICO

DOMANDA N°15

volume di pianificazione (PTV)



Risultati

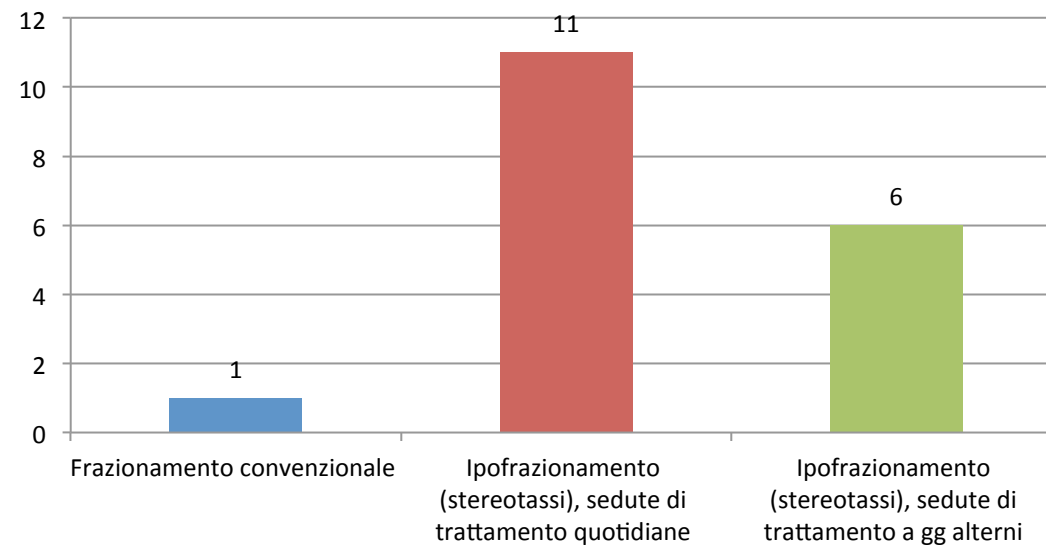


Sessione 2:

TRATTAMENTO RADIOTERAPICO

DOMANDA N°16

Tipo di frazionamento adottato



Risultati

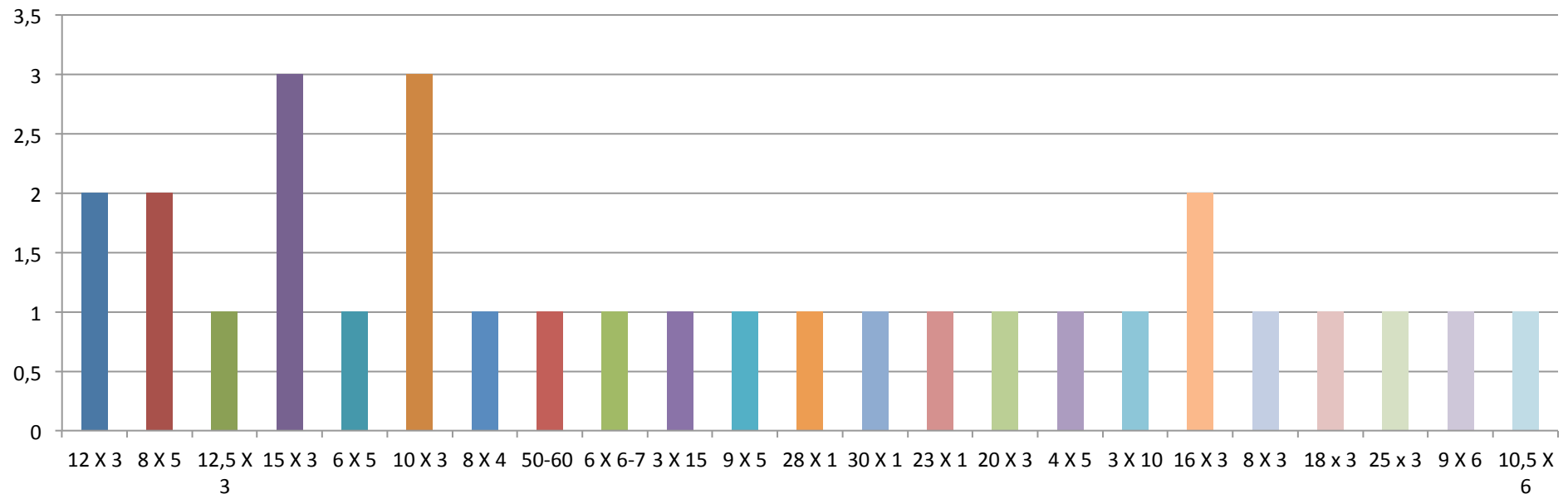


Sessione 2:

TRATTAMENTO RADIOTERAPICO

DOMANDA N°17

Dose di prescrizione
EPATOCARCINOMA



Risultati

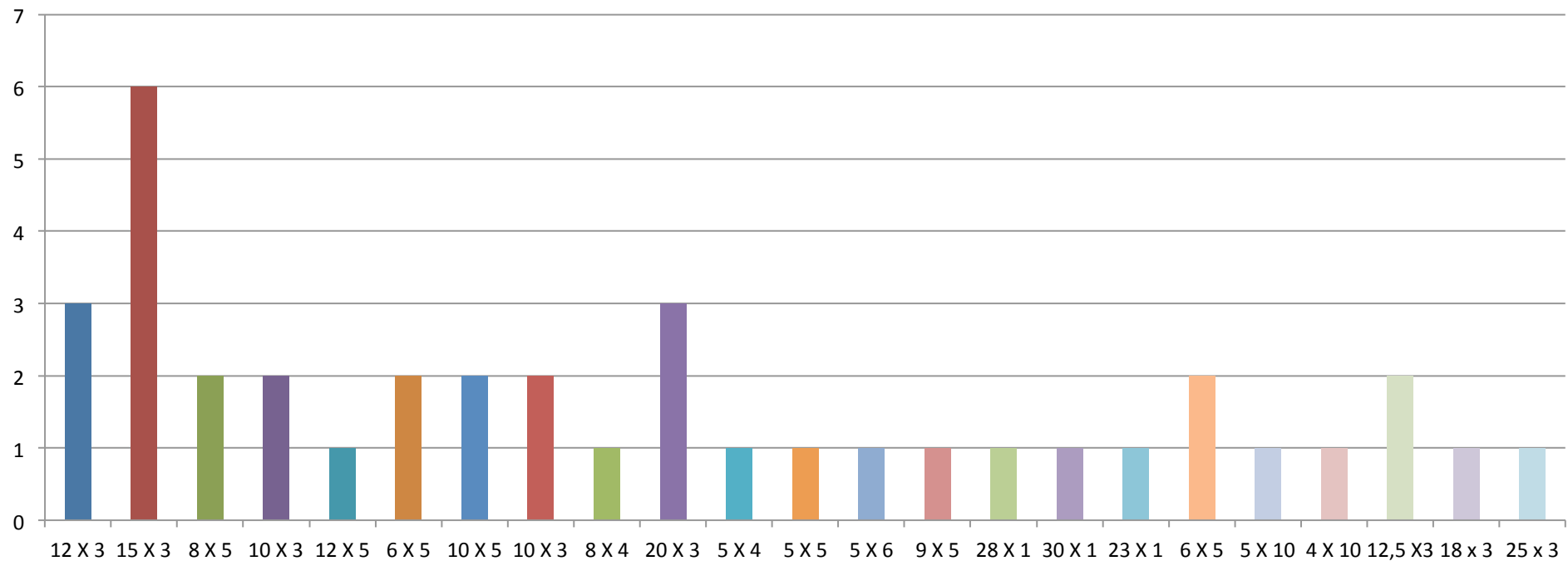


Sessione 2:

TRATTAMENTO RADIOTERAPICO

DOMANDA N°17

Dose di prescrizione
METASTASI EPATICHE



Risultati

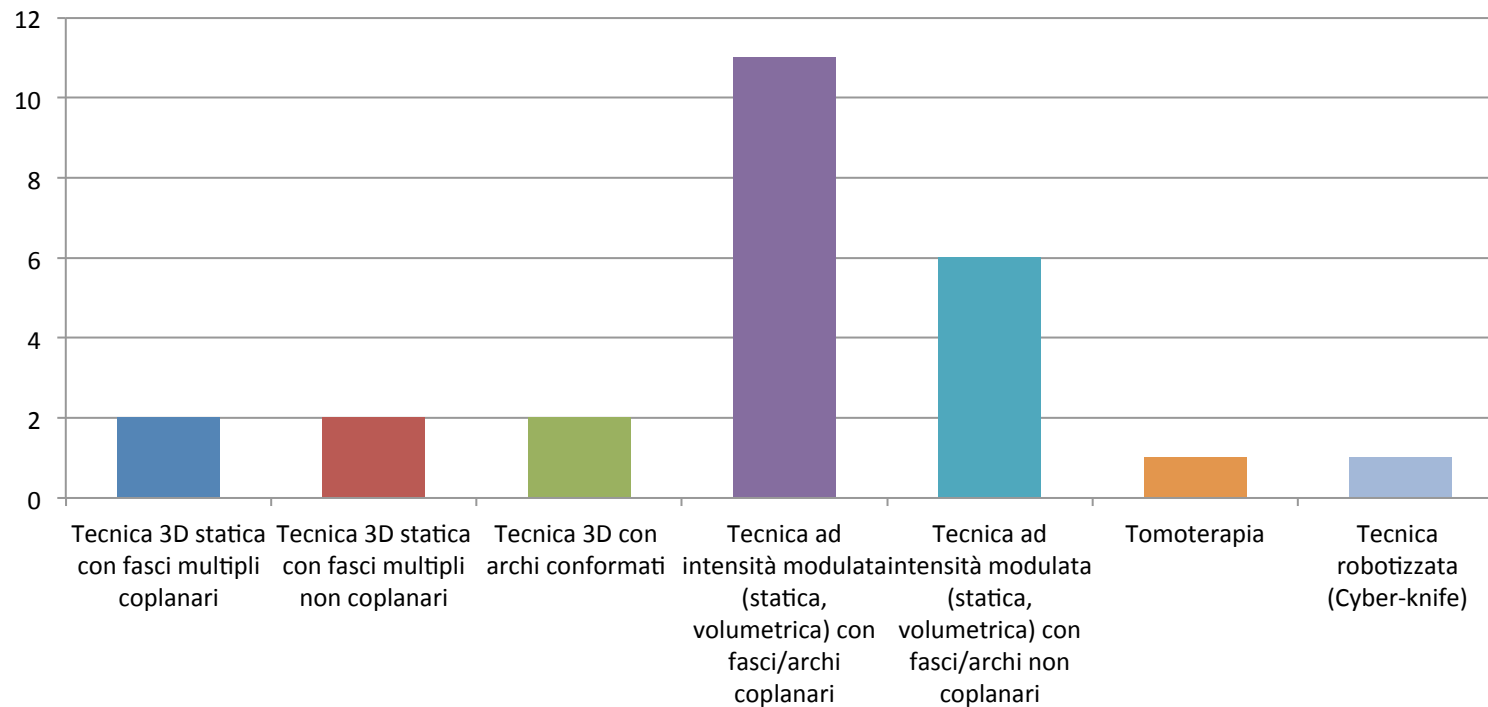


Sessione 2:

TRATTAMENTO RADIOTERAPICO

DOMANDA N°19

Tecnica di
trattamento



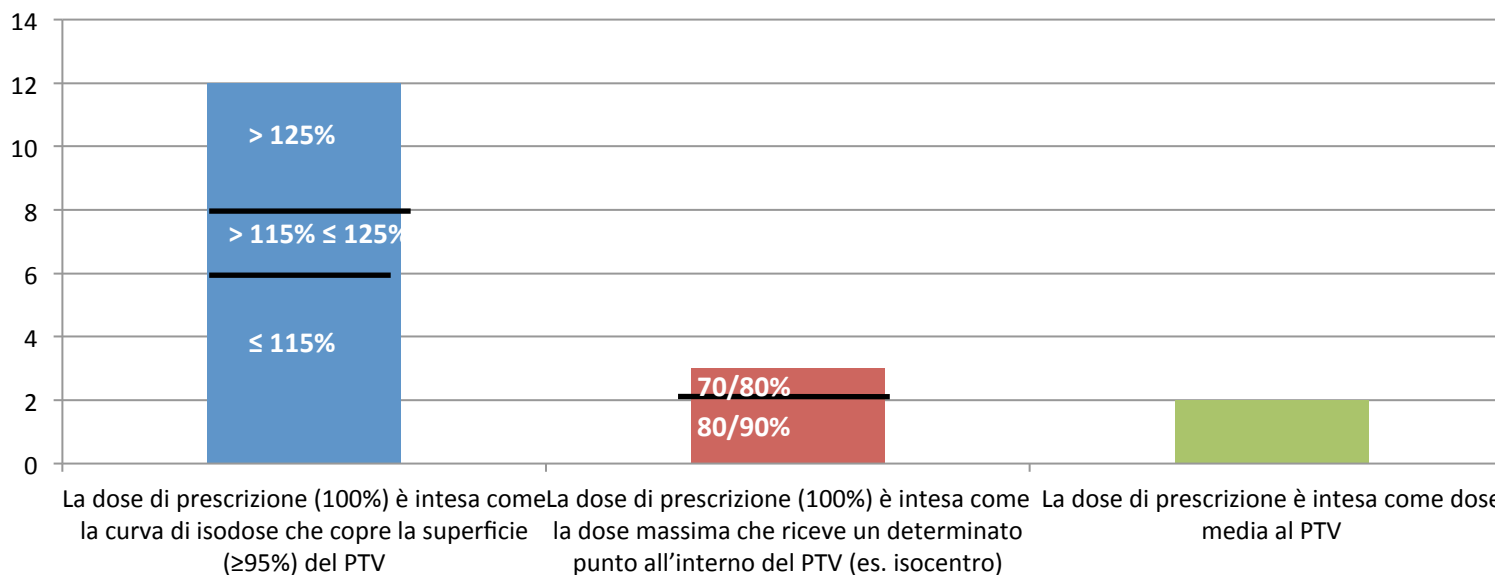
Risultati



Sessione 2:
TRATTAMENTO RADIOTERAPICO

DOMANDA N°20

Modalità di prescrizione



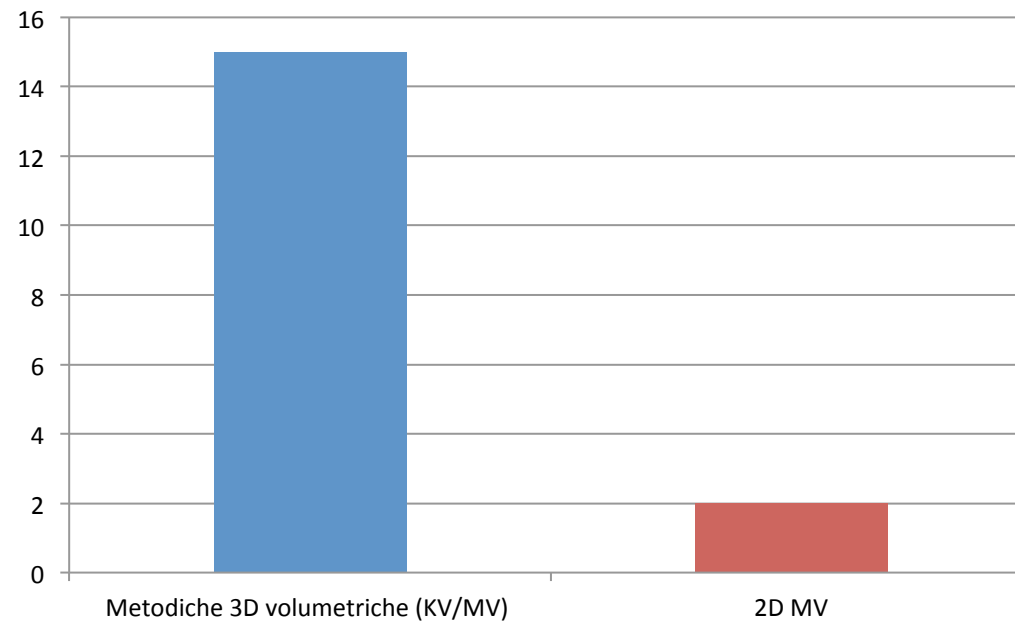
Risultati



Sessione 2:
TRATTAMENTO RADIOTERAPICO

DOMANDA N°21

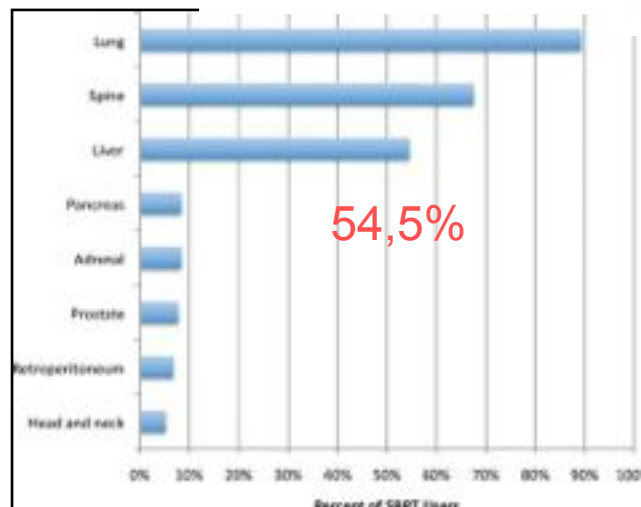
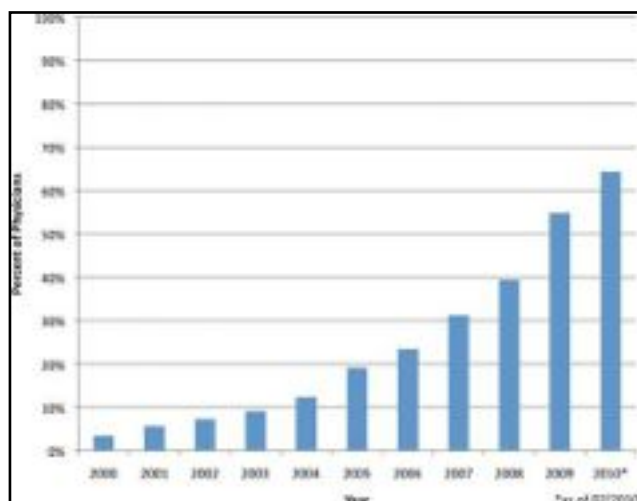
metodiche di IGRT



Discussione

A Survey of Stereotactic Body Radiotherapy Use in the United States

Cancer October 1, 2011



Tumor Site	Fractions (%)	Common Dose/Fraction, Gy (%)	Median Dose/Fraction, Gy (range)	Median IDL, % (range)
Lung (n=262)	3 (47%)	20 (46%), 18 (45%)	18 (10-20)	80 (70-100)
	4 (21%)	12 (78%), 12.5 (11%)	12 (10-16)	85 (80-100)
	5 (30%)	10 (51%), 12 (34%)	10 (3-20)	90 (75-100)
Spine (n=170)	1 (57%)	18 (40%), 16 (34%)	18 (7-24)	85 (70-100)
	3 (22%)	8 (51%), 7 (14%)	8 (6-12)	80 (75-95)
	5 (18%)	6 (60%), 7 (10%)	6 (4-12)	100 (90-100)
Liver (n=142)	3 (48%)	15 (40%), 20 (25%)	15 (8-20)	80 (70-100)
	4 (9%)	12 (77%), 10 (8%)	12 (8-12)	80 (80-95)
	5 (38%)	10 (38%), 12 (19%)	10 (5-12)	90 (70-100)

Liver tumors were treated by 54.5% of SBRT users. The liver was the only disease site in which fiducial markers were used by the majority (56.9%) of respondents. Physicians commonly used respiratory gating (57.9%) or abdominal compression (51.9%) to manage respiratory-induced tumor motion. Alternative methods such as real-time tumor tracking (17.2%) and breath-hold techniques (15.0%) were not commonly used. The most



Associazione Italiana
Radioterapia Oncologica

Gruppo di Studio per i Tumori Gastrointestinali



Azienda Provinciale
per i Servizi Sanitari
Provincia Autonoma di Trento

Discussione

An international survey on liver metastases radiotherapy

MICHAEL I. LOCK¹, MORTEN HOYER², SEAN A. BYDDER³, PAUL OKUNIEFF⁴,
CAROL A. HAHN⁵, ANUSHREE VICHARE⁶ & LAURA A. DAWSON⁷

Supplementary Table Ia. Most commonly used radical liver radiation regimens.

Regimen	Percentage of respondents using regimen
50 Gy/20 daily fractions	3%
60 Gy/30 daily fractions	3%
45 Gy/15 daily fractions	10%
40–50 Gy/5 daily fractions	15%
36–54 Gy/6 daily fractions	5%
45 Gy/3 daily fractions	23%
Other	28%
No radical dose given	13%

Team multidisciplinare: 65%

Discussione



EASL–EORTC Clinical Practice Guidelines: Management of hepatocellular carcinoma[☆]

European Association for the Study of the Liver*, European Organisation for Research and Treatment of Cancer

43 pagine : radioterapia?



11.3. Other loco-regional treatments

The use of conventional external-beam radiation therapy in HCC treatment has been limited by the low radiation tolerance of the cirrhotic liver, which often resulted in radiation-induced liver disease, previously known as radiation-induced hepatitis.³⁰¹ The benefits of external three-dimensional conformal radiotherapy have only been tested in uncontrolled investigations.³⁰² There is no scientific evidence to recommend these therapies as primary treatments of HCC and further research testing modern approaches is encouraged.



Associazione Italiana
Radioterapia Oncologica

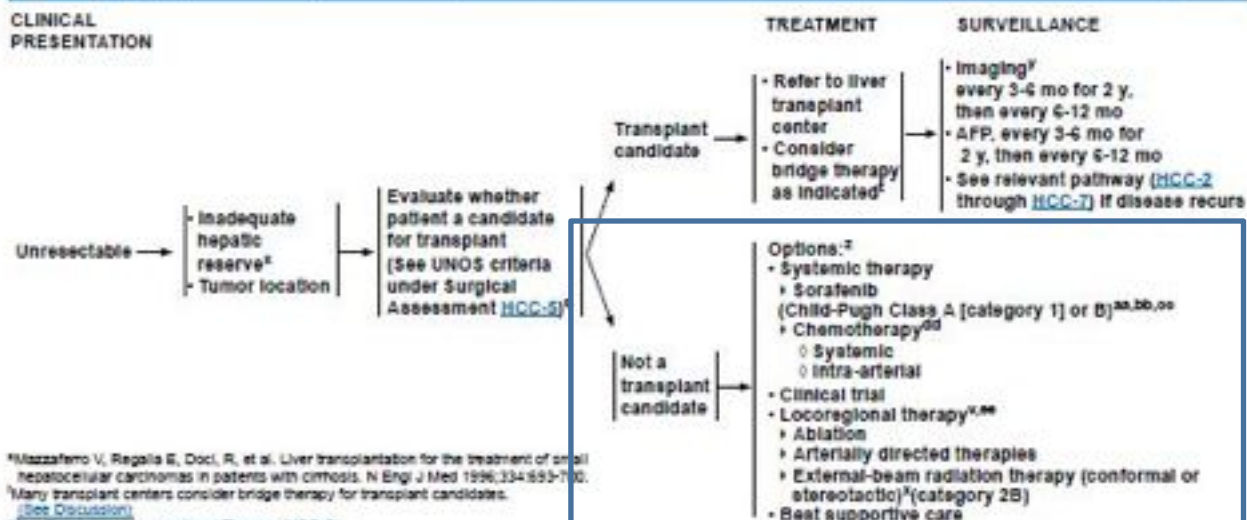
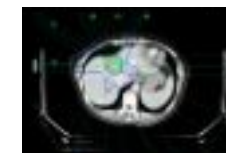
Gruppo di Studio per i Tumori Gastrointestinali

European Journal of Cancer (2012) 48, 599–641



Azienda Provinciale
per i Servizi Sanitari
Provincia Autonoma di Trento

Discussione



^aMazzaferro V, Regalia E, Doczi R, et al. Liver transplantation for the treatment of small hepatocellular carcinomas in patients with cirrhosis. *N Engl J Med* 1996;334:693-700.

^bMany transplant centers consider bridge therapy for transplant candidates.

^cSee [Discussion](#).

^dSee [Principles of Locoregional Therapy \(HCC-6\)](#).

^eCase series and single-arm studies suggest safety and possible efficacy of radiation therapy in selected cases.

^fSee [Principles of Locoregional Therapy \(radiation therapy\) \(HCC-6\)](#).

MRI or multi-phase CT scans for liver assessment are recommended. Consider chest imaging as clinically indicated.

^gOrder does not indicate preference. The choice of treatment modality may depend on extent/location of disease, hepatic reserve, and institutional capabilities.

^hSee [Child-Pugh Score \(HCC-6\)](#).

^{aa}For selected patients, two randomized phase 3 clinical trials have demonstrated survival benefits. (Llovet J, Ricci S, Mazzaferro V, et al. Sorafenib in advanced hepatocellular carcinoma. *N Engl J Med* 2008;359(4):378-390) and (Cheng A, Kang Y, Chen Z, et al. Efficacy and safety of sorafenib in patients in the Asia Pacific region with advanced hepatocellular carcinoma: a phase III randomized, double-blind, placebo-controlled trial. *Lancet Oncol* 2009;10:25-34.)

^{bb}Caution: There are limited safety data available for Child-Pugh Class B or C patients and dosing is uncertain. Use with extreme caution in patients with elevated bilirubin levels. (Miller AA, Murry K, Owsar DR, et al. Phase I and pharmacokinetic study of sorafenib in patients with hepatic or renal dysfunction CALGB 60301. *J Clin Oncol* 2009;27:1800-1805). The impact of sorafenib on patients potentially eligible for transplant is unknown.

^{cc}There are limited data supporting the use of systemic chemotherapy, and its use in the context of a clinical trial is preferred.

^{dd}Use of chemoembolization has also been supported by randomized controlled trials in selected populations over best supportive care. (Lo CM, Ngan H, Tso WK, et al. Randomized controlled trial of transarterial lipiodol chemoembolization for unresectable hepatocellular carcinoma. *Hepatology* 2002;35:1164-1171) and (Llovet JM, Real MI, Montaña X, et al. Arterial embolization or chemoembolization versus symptomatic treatment in patients with unresectable hepatocellular carcinoma: a randomized controlled trial. *Lancet* 2002;359:1734-1739.)

Note: All recommendations are category 2A unless otherwise indicated.
 Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Discussione



NCCN National Comprehensive Cancer Network[®] **NCCN Guidelines Version 2.2014** Hepatobiliary Cancers

[NCCN Guidelines Index](#)
[Hepatobiliary Cancers Table of Contents](#)
[Discussion](#)

CLINICAL PRESENTATION	TREATMENT
<p>Inoperable by performance status or comorbidity, local disease or local disease with minimal extrahepatic disease only</p>	<p>Options:²</p> <ul style="list-style-type: none"> • Sorafenib (Child-Pugh Class A [category 1] or B)^{aa,bb,cc} • Clinical trial • Locoregional therapy^d <ul style="list-style-type: none"> ▶ Ablation ▶ Arterially directed therapies ▶ External-beam radiation therapy (conformal or stereotactic)^e (category 2B) • Best supportive care
<p>Metastatic disease or Extensive liver tumor burden</p>	<p>Options:²</p> <ul style="list-style-type: none"> • Sorafenib (Child-Pugh Class A [category 1] or B)^{aa,bb,cc} • Clinical trial • Best supportive care

^dSee Principles of Locoregional Therapy/Radiation Therapy (HCC-C3).
^eCase series and single-arm studies suggest safety and possible efficacy of radiation therapy in selected cases. (See Principles of Locoregional Therapy/Radiation Therapy (HCC-C3).)
^{aa}Order does not indicate preference. The choice of treatment modality may depend on extent/location of disease, hepatic reserve, and institutional capabilities.
^{bb}See Child-Pugh Score (HCC-A).
^{cc}For selected patients, two randomized phase 3 clinical trials have demonstrated survival benefits. (Llovet J, Ricci S, Mazzaferro V, et al. Sorafenib in advanced hepatocellular carcinoma. *N Engl J Med* 2008;359(4):378-390) and (Cheng A, Kang Y, Chen Z, et al. Efficacy and safety of sorafenib in patients in the Asia-Pacific region with advanced hepatocellular carcinoma: a phase III randomized, double-blind, placebo-controlled trial. *Lancet Oncol* 2009;10:25-34).
^{dd}Caution: There are limited safety data available for Child-Pugh Class B or C patients and dosing is uncertain. Use with extreme caution in patients with elevated bilirubin levels. (Miller AA, Murry K, Owzar DR, et al. Phase I and pharmacokinetic study of sorafenib in patients with hepatic or renal dysfunction: CALGB 60301. *J Clin Oncol* 2009;27:1800-1805). The impact of sorafenib on patients potentially eligible for transplant is unknown.

Note: All recommendations are category 2A unless otherwise indicated.
 Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Version 2.2014 04/20/14 © National Comprehensive Cancer Network, Inc. 2014. All rights reserved. The NCCN Guidelines[®] and this illustration may not be reproduced in any form without the express written permission of NCCN[®].

HCC-7

Discussione



NCCN

National
Comprehensive
Cancer
Network®

NCCN Guidelines Version 1.2015

Rectal Cancer

Colon Cancer

[NCCN Guidelines Index](#)
[Rectal Cancer Table of Contents](#)
[Discussion](#)

PRINCIPLES OF RADIATION THERAPY

- Radiation therapy fields should include the tumor or tumor bed, with a 2–5 cm margin, the presacral nodes, and the internal iliac nodes. The external iliac nodes should also be included for T4 tumors involving anterior structures.
- Multiple radiation therapy fields should be used (generally a 3- or 4-field technique). Positioning and other techniques to minimize the volume of small bowel in the fields should be encouraged.
- For postoperative patients treated by abdominoperineal resection, the perineal wound should be included within the fields.
- Intensity-modulated radiation therapy (IMRT) should only be used in the setting of a clinical trial or in unique clinical situations including re-irradiation of recurrent disease after previous radiotherapy.
- Radiation doses:
 - ▶ 45–50 Gy in 25–28 fractions to the pelvis.
 - ▶ For resectable cancers, after 45 Gy a tumor bed boost with a 2-cm margin of 5.4 Gy in 3 fractions could be considered for preoperative radiation and 5.4–9.0 Gy in 3–5 fractions for postoperative radiation.
 - ▶ Small bowel dose should be limited to 45 Gy.
- Intraoperative radiation therapy (IORT), if available, should be considered for very close or positive margins after resection, as an additional boost, especially for patients with T4 or recurrent cancers. If IORT is not available, 10–20 Gy external beam radiation and/or brachytherapy to a limited volume could be considered soon after surgery, prior to adjuvant chemotherapy.
- For unresectable cancers, doses higher than 54 Gy may be required, if technically feasible.
- 5-fluorouracil-based chemotherapy should be delivered concurrently with radiation therapy.
- In patients with a limited number of liver or lung metastases, radiotherapy can be considered in highly selected cases or in the setting of a clinical trial. Radiotherapy should not be used in the place of surgical resection. Radiotherapy should be delivered in a highly conformal manner. The techniques can include 3-D conformal radiotherapy, IMRT, or stereotactic body radiation therapy (SBRT). (category 3)
- Side effect management:
 - Female patients should be considered for vaginal dilators and instructed on the symptoms of vaginal stenosis.
 - Male patients should be counseled on infertility risks and given information regarding sperm banking.
 - Female patients should be counseled on infertility risks and given information regarding oocyte, egg, or ovarian tissue banking prior to treatment.



Associazione Italiana
Radioterapia Oncologica

Gruppo di Studio per i Tumori Gastrointestinali

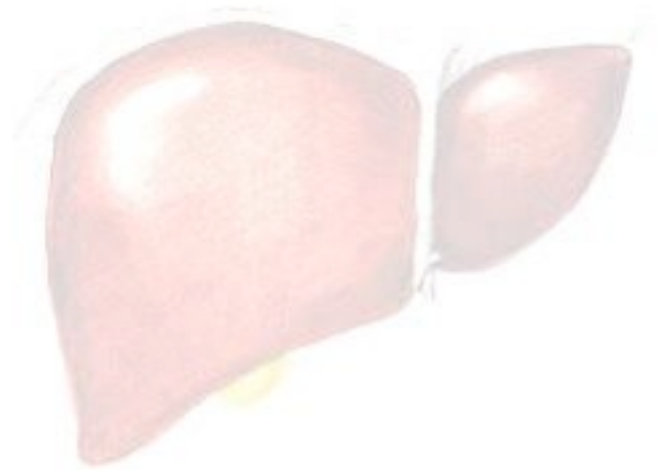


Azienda Provinciale
per i Servizi Sanitari
Provincia Autonoma di Trento

Conclusioni



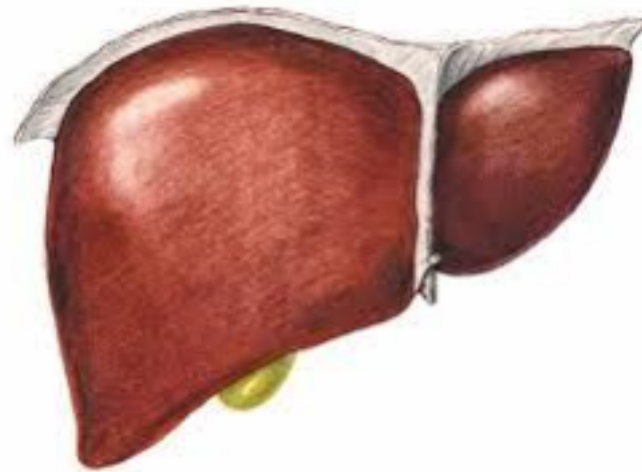
“Abbiamo Fegato?”





Conclusioni

“Abbiamo Fegato?”



Creazione gruppo di lavoro per

- Omogeneizzazione trattamenti
- Integrazione con altre terapie
- Condivisione proposte di studio
- Raccolta ed analisi casistica multicentrica
-

GRUPPI DI STUDIO		
	12.00 - 12.30	
AULA VESALIO	Costituzione Gruppo di Studio Re-Irradiazione Coordinatore: V. Donato	
	12.30 - 14.30	14.30 - 16.30
AULA MORGAGNI	Cure Palliative	Prostata
AULA VESALIO	Mammella	Polmone
AULA GIOTTO	Testa-collo	Brachiterapia
AULA CARRARESI	Gastroenterico	IORT
AULA PALLADIO	Cerebrali	Radioterapia metabolica

Ringraziamenti

GRUPPO FEGATO

R. NIESPOLO

A. GUARNERI

V. DELL'ACQUA

MC LEONARDI



Associazione Italiana
Radioterapia Oncologica

Gruppo di Studio per i Tumori Gastrointestinali

	<i>Nome</i>
<i>Coordinatore</i>	Giovanna Mantello
<i>Vice-coordinatore</i>	Francesca Valvo
<i>Consigliere</i>	Gian Carlo Mattiucci
<i>Consigliere</i>	Vincenzo Fusco
<i>Consigliere</i>	Luciana Caravatta (segretario)



Associazione Italiana di Radioterapia Oncologica



Associazione Italiana
Radioterapia Oncologica

Gruppo di Studio per i Tumori Gastrointestinali



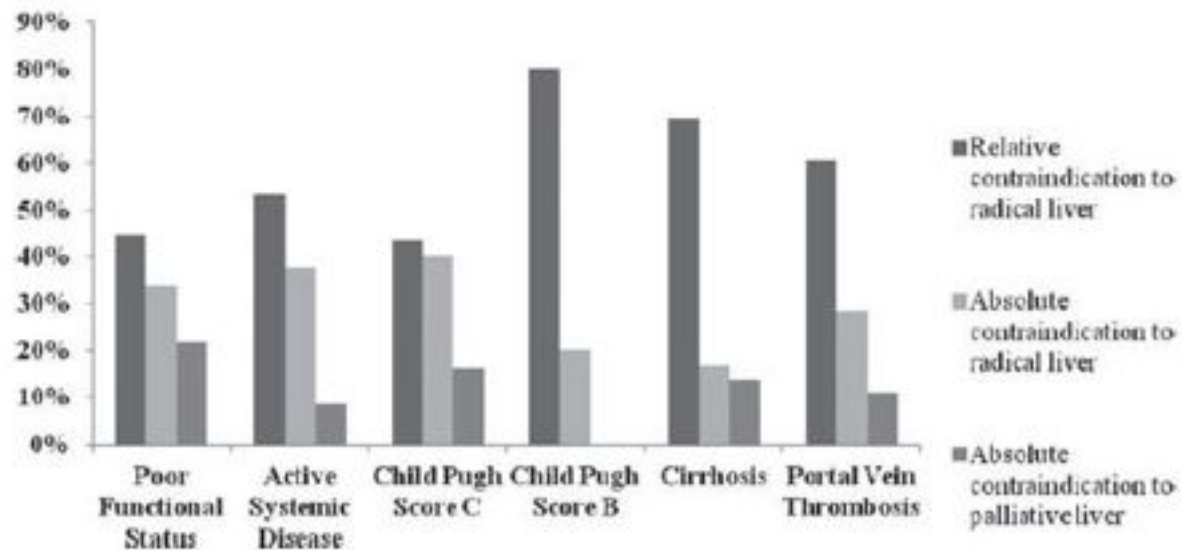
Azienda Provinciale
per i Servizi Sanitari
Provincia Autonoma di Trento

Per discussione

Discussione

An international survey on liver metastases radiotherapy

MICHAEL I. LOCK¹, MORTEN HOYER², SEAN A. BYDDER³, PAUL OKUNIEFF⁴,
CAROL A. HAHN⁵, ANUSHREE VICHARE⁶ & LAURA A. DAWSON⁷



suggest to the authors that an expert consensus and clinical trials are needed to provide guidance to referring physicians and radiation oncologists if radiation oncology is to establish itself as an accepted treatment modality in this area.



Associazione Italiana
Radioterapia Oncologica

Gruppo di Studio per i Tumori Gastrointestinali



*Azienda Provinciale
per i Servizi Sanitari
Provincia Autonoma di Trento*

Cronoprogramma



- 1) Giugno 2014: invio ai Centri, pubblicazione su Sito AIRO
- 2) Giugno-settembre 2014: invio delle risposte da parte dei Centri con solleciti da parte del gruppo a direttori dei centri e referenti GI
- 3) Ottobre 2014: raccolta, analisi ed elaborazione dei dati.

Indagine Conoscitiva Radioterapia Fegato

Il Gruppo di Studio AIRO dei Tumori Gastrointestinali ha proposto un'indagine conoscitiva riguardante il ruolo che il radioterapista oncologo riveste nei Centri italiani nel trattamento della malattia neoplastica a localizzazione epatica (epatocarcinoma e metastasi epatiche).

Di seguito sono scaricabili il questionario, la lettera con le indicazioni del Gruppo GI ed il cronoprogramma.

Il questionario compilato potrà essere inviato all'indirizzo mail del Dott. Francesco Dionisi: francescodionisi2@gmail.com

File allegati:

- Questionario
- Lettera
- Cronoprogramma

NCCN COLON EVIDENZA 3

Opzioni di trattamento non chirurgiche:

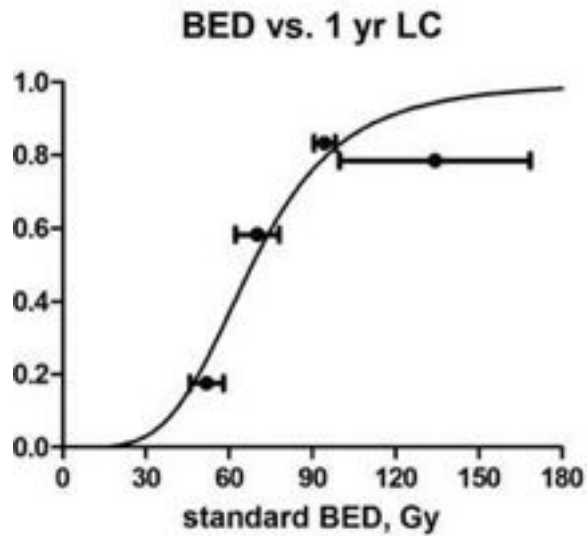
RFA

STUDY	NO. OF PATIENTS	ACCESS	SIZE, CM	NO. OF TUMORS	MEDIAN SURVIVAL, MONTHS	OVERALL SURVIVAL RATE AT 3 YEARS AND 5 YEARS
Solbiati 2001 ¹⁰⁷	117	Percutaneous (P)	2.8		36	
Gillams 2004 ¹⁰¹	167	P	3.9	4.1	32	3-y: 40% 5-y: 17%
Lencioni 2004 ⁹⁶	423	P	2.7	1.4	25	3-y: 47% 5-y: 24%
De Baere 2003 ¹⁰⁰	155	P	2.5	1.3	27	3-y: 31%
Solbiati 2006 ¹⁰⁶	121	P	2.1	2.1	47	3-y: 60% 5-y: 35%
Pereira 2006 ¹⁰⁴	177	P	2.2	2.2		3-y: 71% 5-y: 55%
Siperstein 2007 ¹⁰⁵	235	Laparoscopic (L)	3.9	2.8	24	3-y: 20% 5-y: 18%
Machi 2006 ⁴⁷	100	P, L, open (O)	3.0	3.5	28	3-y: 42% 5-y: 31%
Iannitti 2002 ¹⁰³	52	P, L, O	5.2			3-y: 50%
Hildebrand 2006 ¹⁰²	56	P, L, O	3.5	3.5	28	3-y: 42%
Abdalla 2004 ⁹⁹	57	O	2.5	1.7		3-y: 37% 4-y: 22%
Yu 2006 ⁵¹	50	O	4.2	3.3	37	3-y: 52% 5-y: 32%

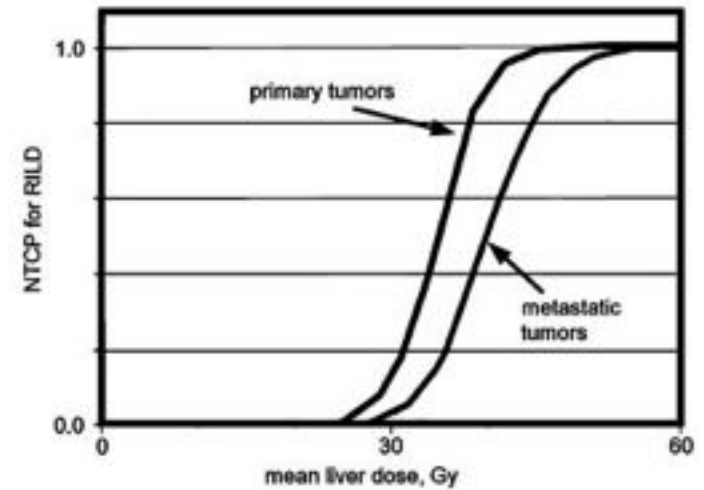
Timmerman et al Ca Cancer J Clin 2009

Risultati migliori in lesioni < 3cm e lontano grossi vasi
sede centrale, sottocapsulare: non indicata

Background



Chang et al Cancer 2011



Dawson et al IJROBP0 2002

**STEREOTACTIC HIGH DOSE FRACTION RADIATION THERAPY OF
EXTRACRANIAL TUMORS USING AN ACCELERATOR**

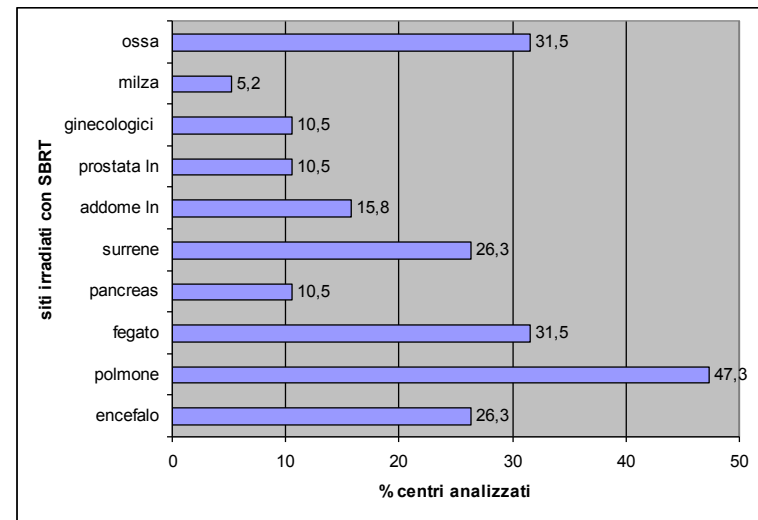
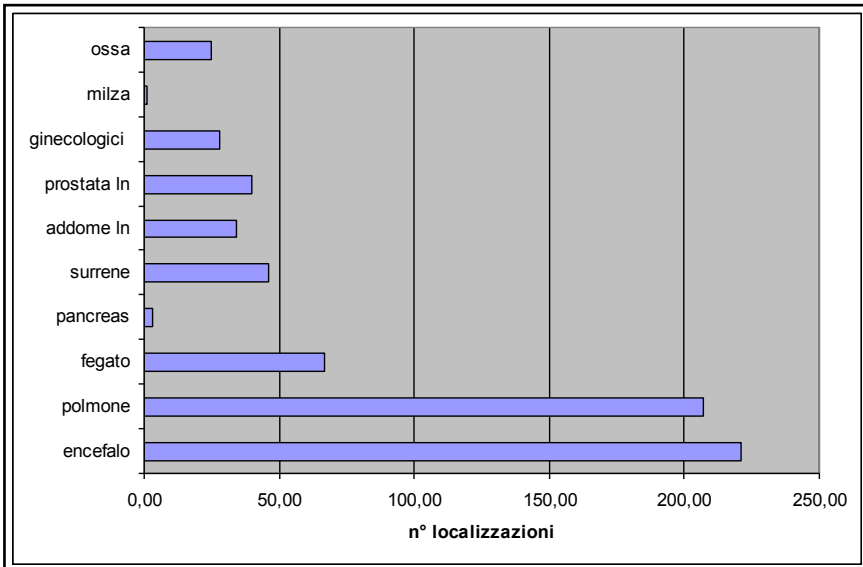
Clinical experience of the first thirty-one patients

1995

HENRIC BLOMGREN, INGMAR LAX, INGEMAR NÄSLUND and RUT SVANSTRÖM

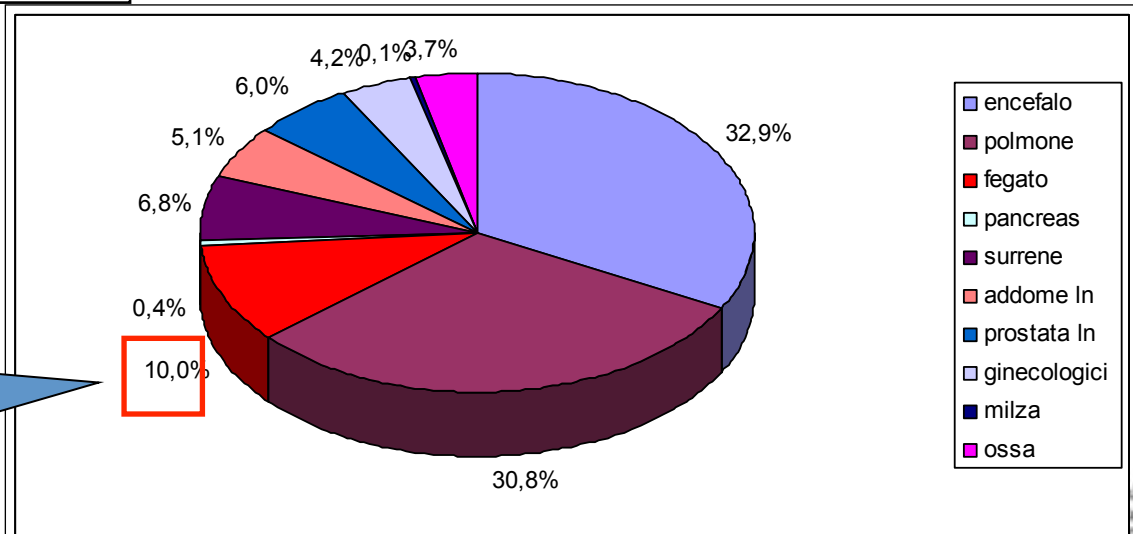
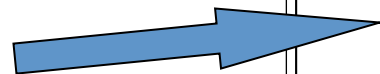


Background



RADIOTHERAPY OF OLIGOMETASTATIC DISEASES

19 centri
522 pazienti
672 localizzazioni



Risultati



Sessione 1:

PRESA IN CURA-APPROCCIO MULTIDISCIPLINARE

DOMANDA N°2

Affluiscono presso la tua Struttura Sanitaria pazienti affetti da epatocarcinoma non metastatico o neoplasia epatica secondaria?

