La gestione delle interruzioni in corso di terapia

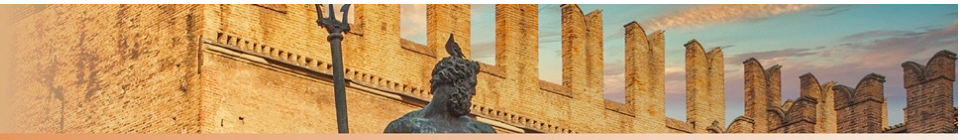
Francesco Deodato

UOC Radioterapica Oncologica 'Molise ART'

Gemelli Molise, Campobasso – Università Cattolica S. Cuore, Roma

Associazione Italiana Radioterapia e Oncologia clinica

Società Italiana di Radiobiologia



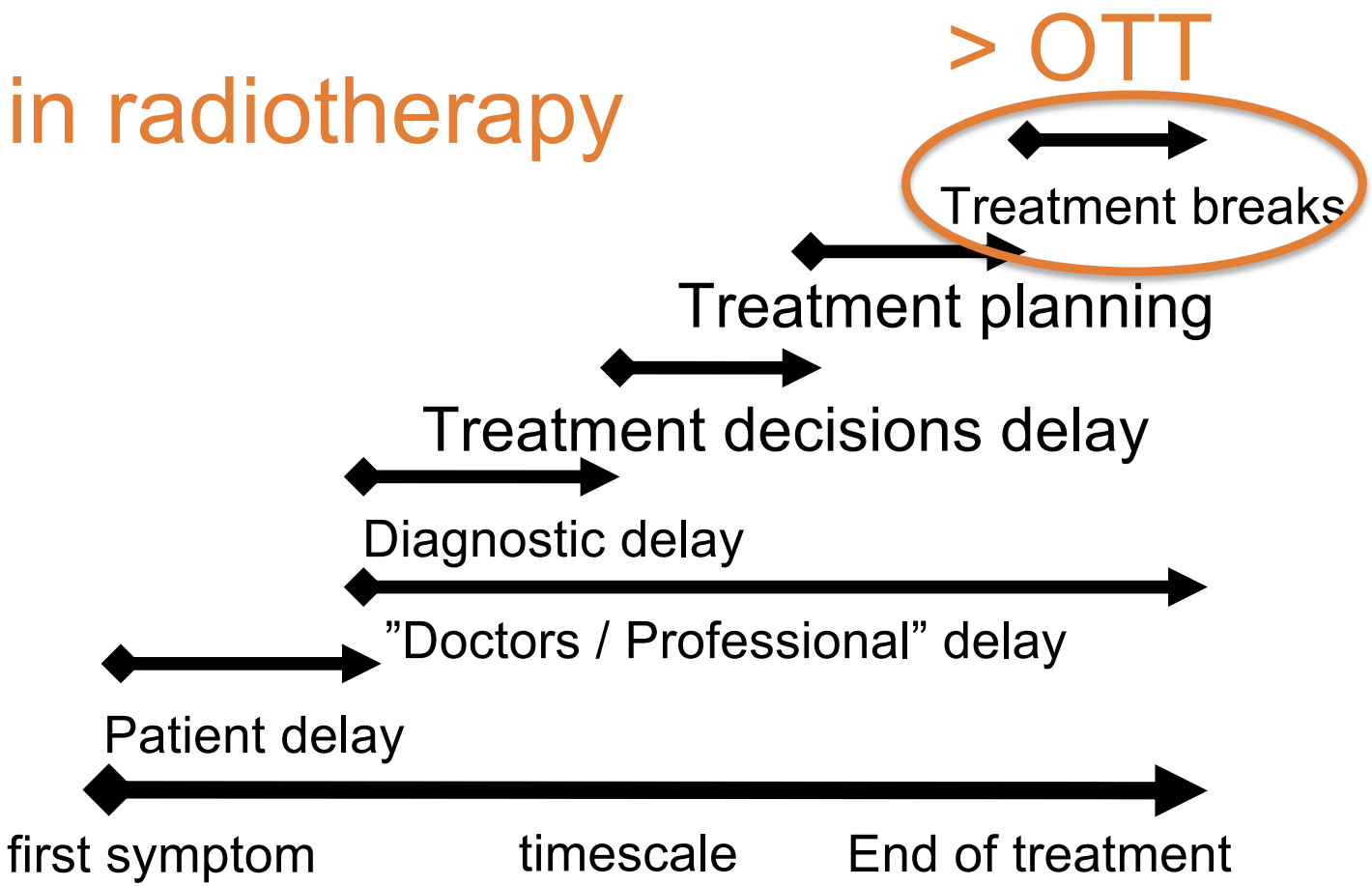
DICHIARAZIONE

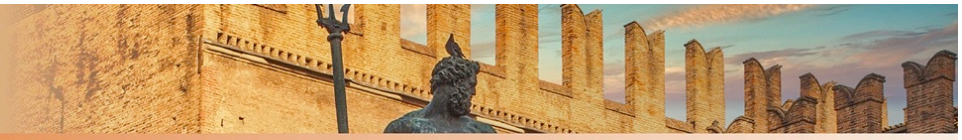
Relatore: Francesco Deodato

Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario: **NIENTE DA DICHIARARE**
- Consulenza ad aziende con interessi commerciali in campo sanitario : **NIENTE DA DICHIARARE**
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario : **NIENTE DA DICHIARARE**
- Partecipazione ad Advisory Board: **NIENTE DA DICHIARARE**
- Titolarità di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario: **NIENTE DA DICHIARARE**
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario: **NIENTE DA DICHIARARE**
- Altro: **NIENTE DA DICHIARARE**

Waiting time in radiotherapy





> OTT ⟶ detrimental impact on tumor control

- Repopulation of cancer stem cells
- Increasing hypoxia
- Evolution of radiation resistant clones / cancer stem cells

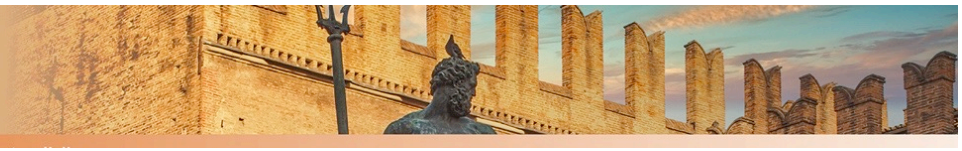


Table 4. Radiotherapy treatment—University of Louisville (July 1984 through June 1985): Cause of interruption according to primary site

Cause of interruptions	Head and neck												Total (%)
Rest	45												47 (27.8)
Transportation													12 (7.1)
Snow	5												20 (11.8)
Machine down	1												11 (6.5)
Undocumented	4												10 (5.9)
Miscellaneous	7												17 (10.1)
Non-compliant	6												16 (9.5)
Patient request	3												5 (3.0)
Patient death	2												15 (8.8)
													7 (4.1)
													9 (5.3)
													169
Total patients	73	34	62	47	(24.1)		(14.1)		(24.1)				

isville (July 1984 through June 1985): Reason for rest

interruption in days

6–10 11–15 >15

records).

361

Table 6. Radiotherapy treatment—University of Louisville (July 1984 through June 1985): Duration of interruptions according to primary site

Primary site	Duration of interruption in days					Total patients
	1	2–5	6–10	11–15	>15	
Head and neck	5	17	26	9	16	73
Breast	4	6	14	4	6	34
Lung	9	19	9	13	12	62
Gyn	5	6	10	5	21	47

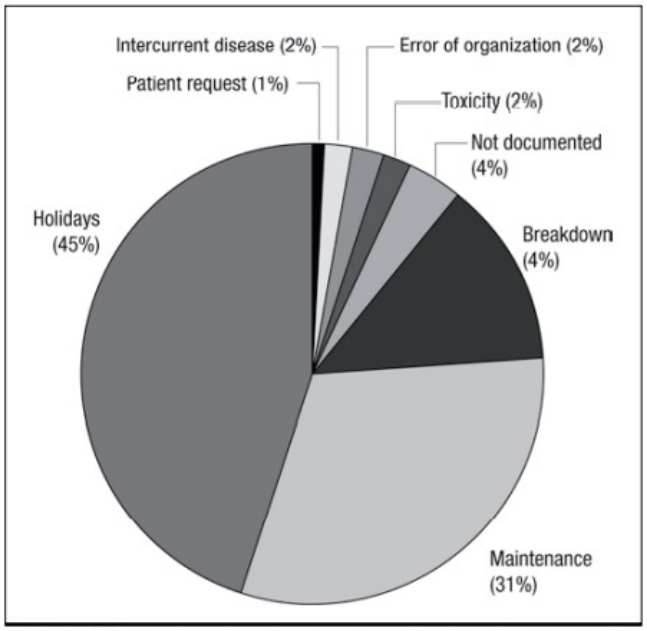
al (%)

9 (46.8)
2 (3.3)
1 (5.8)
3 (3.6)
5 (9.7)
0 (11.1)
4 (3.9)
3 (5.0)
9 (10.8)

* Treatment interrupted due to unusually adverse tissue reactions.
† Most patients died during the first week of treatment.

478 pts (curative intent)
194 breast Cancer
58 lung cancer
55 prostate cancer
47 H&N cancer
30 GI cancer
30 Gyn cancer
21 NHD
18 Brain tumors
25 Miscellaneous

76.6%
of unplanned
interruptions



GAP duration(days)	1	2	3	4	5	6	7	8	9	>10
HOLIDAYS	516	16								
MAINTENANCE	346	6			1		7		1	1
MACHINE DOWN	100	27	9	5	3	1	4	3		2
OTHERS	74	13	4	3	4		2	2	1	12

Fig. 5 Cause and duration of interruptions

17.4% of pts had interruptions more than 5 days
5.6% had interruptions more than 10 days

ent time (OTT)
ractice and impact
interruptions

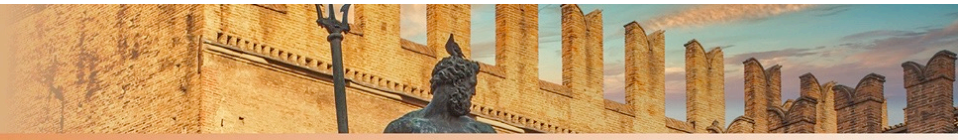
Carlota Monfà Binefa ·

Only 23.4% of pts end their treatment in the planned OTT

Garau et al. Clin Trans Oncol 2009

Unplanned interruptions in RT: management

- Maintaining OTT and dose per fraction and total dose
  - RT on Saturday
  - RT twice per day on the day after the interruption, 6–8 hours apart to allow for sublethal damage repair
- Maintaining OTT but increasing dose per fraction
- Prolongation OTT with extra dose to compensate for the gap

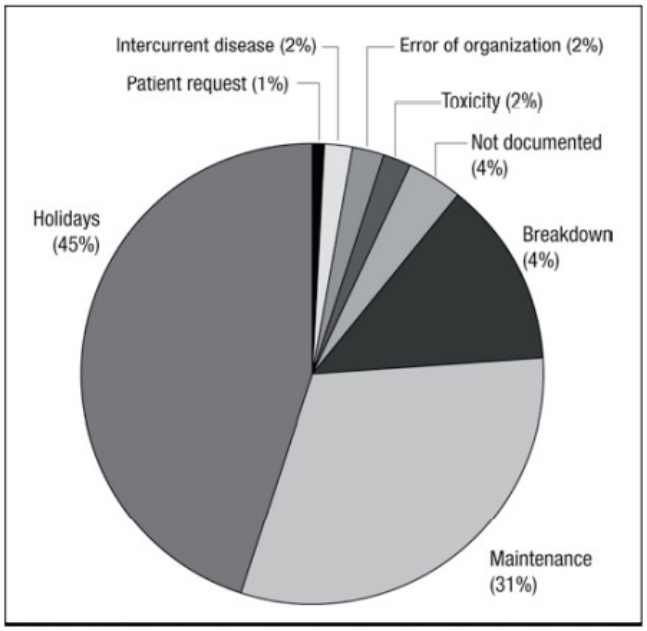


Unplanned interruptions in RT: management

- Maintaining OTT and dose per fraction and total dose
  - RT on Saturday
  - RT twice per day on the day after the interruption, 6–8 hours apart to allow for sublethal damage repair
- Maintaining OTT but increasing dose per fraction
- Prolongation OTT with extra dose to compensate for the gap

478 pts (curative intent)
194 breast Cancer
58 lung cancer
55 prostate cancer
47 H&N cancer
30 GI cancer
30 Gyn cancer
21 NHD
18 Brain tumors
25 Miscellaneous

76.6%
of unplanned
interruptions



GAP duration(days)	1	2	3	4	5	6	7	8	9	>10
HOLIDAYS	516	16								
MAINTENANCE	346	6			1		7		1	1
MACHINE DOWN	100	27	9	5	3	1	4	3		2
OTHERS	74	13	4	3	4		2	2	1	12

Fig. 5 Cause and duration of interruptions

17.4% of pts had interruptions more than 5 days
5.6% had interruptions more than 10 days

Only 23.4% of pts end their treatment in the planned OTT

Garau et al. Clin Trans Oncol 2009

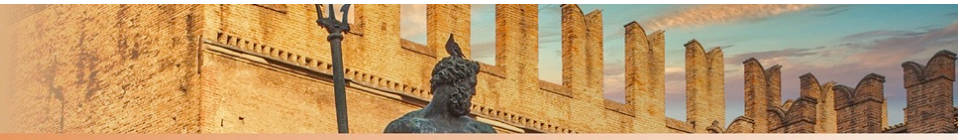
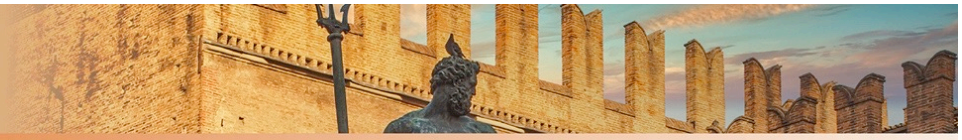


Table 3 Proportion of patients who finished their radiotherapy in the planned time and average excess days by site

	Normal practice		Recalculations–Saturday	
	% of patients	Days in excess	% of patients	Days in excess
Breast cancer	17.5	3.7	11.8	4.2
Lung cancer	25.8	2.4	15.5	3.6
Prostate cancer	3.6	4	0	5.8
H & N cancer	48.9	1.9	19.5	3.9
Gynaecol. cancer	23.3	3.7	7.2	4.4
Cervical cancer	14.4	4	10	4.6
Gastrointest. cancer	36.6	2.1	23.3	3.1
NHL & Hodgkin's disease	57.1	2.2	19	2.9
CNS tumours & PCI	27.7	1.7	27.7	1.8
Miscel.	12	5.5	4	6.9

Garau et al. Clin Trans Oncol 2009



Unplanned interruptions in RT: management

- Maintaining OTT and dose per fraction and total dose
  - RT on Saturday
  - RT twice per day on the day after the interruption, 6–8 hours apart to allow for sublethal damage repair
- Maintaining OTT but increasing dose per fraction
- Prolongation OTT with extra dose to compensate for the gap

Unplanned interruptions in RT: management

- Maintaining OTT and dose per fraction and total dose
  - RT on Saturday
  - RT twice per day on the day after the interruption, 6–8 hours apart to allow for sublethal damage repair
- Maintaining OTT but increasing dose per fraction
- Prolongation OTT with extra dose to compensate for the gap

Table 10.1 Fractionation sensitivity of human normal tissues and tumours

Tissue/organ	Endpoint	α/β (Gy)	95% CL (Gy)	Source
Early reactions				
Skin	Erythema	8.8	[6.9; 11.6]	Turesson and Thames (1989)
	Erythema	12.3	[1.8; 22.8]	Bentzen et al. (1988)
	Dry desquamation	~8	N/A	Chogule and Supe (1993)
	Desquamation	11.2	[8.5; 17.6]	Turesson and Thames (1989)
Oral mucosa	Mucositis	9.3	[5.8; 17.9]	Denham et al. (1995)
	Mucositis	15	[−15; 45]	Rezvani et al. (1991)
	Mucositis	~8	N/A	Chogule and Supe (1993)
Late reactions				
Skin/vasculature	Telangiectasia	2.8	[1.7; 3.8]	Turesson and Thames (1989)
	Telangiectasia	2.6	[2.2; 3.3]	Bentzen et al. (1990)
	Telangiectasia	2.8	[−0.1; 8.1]	Bentzen and Overgaard (1991)
	Telangiectasia	3.8	[1.8; 5.7]	Haviland et al. (2013)
Subcutis	Fibrosis	1.7	[0.6; 2.6]	Bentzen and Overgaard (1991)
Breast	Cosmetic chang			
	Induration (fibr			
	Breast oedema			
Muscle/vasculature/cartilage	Impaired shoul			
Nerve	Brachial plexop			
	Brachial plexop			
	Optic neuropat			
Spinal cord	Myelopathy			
Eye	Corneal injury			
Bowel	Stricture/perfor			
Bowel	Various late eff			
Lung	Pneumonitis			
	Lung fibrosis (r			
Head and neck	Various late eff			
	Various late eff			
Supraglottic larynx	Various late eff			
Oral cavity + oroph.	Various late eff			
Tumours				
Head and neck				
Various				
Larynx				
Vocal cord				
Buccal mucosa		6.6	[2.9; infinity]	Maciejewski et al. (1989)
Tonsil		7.2	[3.6; infinity]	Maciejewski et al. (1989)
Nasopharynx		16	[−11; 43]	Lee et al. (1995)
Lung (NSCLC, early)		8.2	[7.0; 9.4]	Stuschke and Pöttgen (2010)
Skin		8.5[a]	[4.5; 11.3]	Trott et al. (1984)
Prostate[b]		2.7	[1.6; 3.8]	Vogelius and Bentzen (2018)(26)
Breast		3.5	[1.2; 5.7]	Haviland et al. (2013)
Oesophagus		4.9	[1.5; 17]	Geh et al. (2006)
Melanoma		0.6	[−1.1; 2.5]	Bentzen et al. (1989)
Liposarcoma		0.4	[−1.4; 5.4]	Thames and Suit (1986)

Note: Reference details are available from Søren Bentzen. See also (25) and Table 14.2 in this book.

[a] Re-analysis of original published data.

[b] Meta-analysis of randomized controlled trials of external beam therapy, more estimates are available from comparisons of outcome after brachytherapy versus external beam therapy. This analysis includes an adjustment for overall treatment time, see Table 10.3.

$$EQD2_{\alpha/\beta} = D\frac{d+(\alpha/\beta)}{2\ \text{Gy}+(\alpha/\beta)}$$

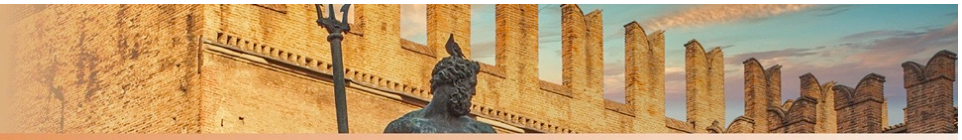
Tumours

Head and neck		
Various	10.5	[6.5; 29]	Stuschke and Thames (1999)
Larynx	14.5[a]	[4.9; 24]	Rezvani et al. (1993)
Vocal cord	~13	'Wide'	Robertson et al. (1993)
Buccal mucosa	6.6	[2.9; infinity]	Maciejewski et al. (1989)
Tonsil	7.2	[3.6; infinity]	Maciejewski et al. (1989)
Nasopharynx	16	[−11; 43]	Lee et al. (1995)
Lung (NSCLC, early)	8.2	[7.0; 9.4]	Stuschke and Pöttgen (2010)
Skin	8.5[a]	[4.5; 11.3]	Trott et al. (1984)
Prostate[b]	2.7	[1.6; 3.8]	Vogelius and Bentzen (2018)(26)
Breast	3.5	[1.2; 5.7]	Haviland et al. (2013)

Joiner et Kogel. Basic Clinical Radiobiology. 5° Edition, 2019

Unplanned interruptions in RT: management

- Maintaining OTT and dose per fraction and total dose
  - RT on Saturday
  - RT twice per day on the day after the interruption, 6–8 hours apart to allow for sublethal damage repair
- Maintaining OTT but increasing dose per fraction
- Prolongation OTT with extra dose to compensate for the gap



Unplanned interruptions in RT: management

- Maintaining OTT and dose per fraction and total dose
  - RT on Saturday
  - RT twice per day on the day after the interruption, 6–8 hours apart to allow for sublethal damage repair
- Maintaining OTT but increasing dose per fraction
- Prolongation OTT with extra dose to compensate for the gap

$$EQD2_T = EQD2_t - (T - t) \cdot D_{prolif}$$

Table 10.3 Values for D_{prolif} from clinical studies

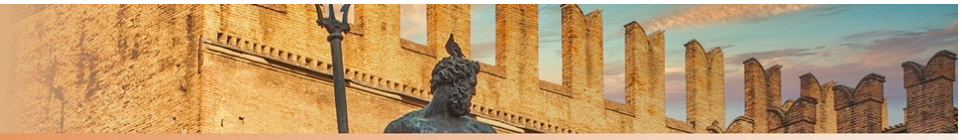
Tissue	Endpoint	D_{prolif} (Gy day^{-1})	95% CL (Gy day^{-1})	T_k[b] (days)	Source
Early reactions					
Skin	Erythema	0.12	[−0.12; 0.22]	<12	Bentzen et al. (2001)
Mucosa	Mucositis	0.8	[0.7; 1.1]	<12	Bentzen et al. (2001)
Lung	Pneumonitis	0.54	[0.13; 0.95]		Bentzen et al. (2000)[a]
Tumours					
Head and neck					
Larynx		0.74	[0.30; 1.2]		Robertson et al. (1998)
Tonsils		0.73		30	Withers et al. (1995)
Various		0.8	[0.5; 1.1]	21	Robers et al. (1994)
Various		0.64	[0.42; 0.86]		Hendry et al. (1996)[a]
Breast		0.60	[0.10; 1.18]		Haviland et al. (2016)
Oesophagus		0.59	[0.18; 0.99]		Geh et al. (2005)
Non-small cell lung cancer		0.45	N/A		Koukourakis et al. (1996)
Medulloblastoma		0.52	[0.29; 0.75]	0 or 21	Hinata et al. (2001)
Prostate		0.24	[0.03; 0.44]	52	Thames et al. (2010)

Note: Reference details are available from Søren Bentzen.

[a] Pooled estimate from a review of studies in the literature.

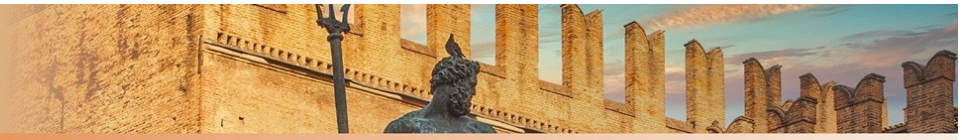
[b] T_k is the assumed time for the onset of accelerated proliferation.

Joiner et Kogel. Basic Clinical Radiobiology. 5° Edition, 2019



Active measures recommended to maintain the prescribed OTT (1)

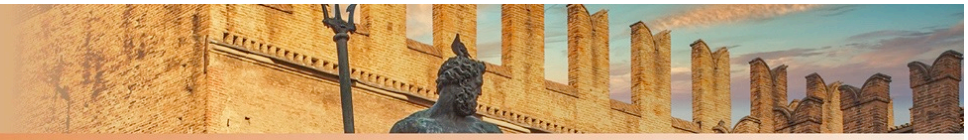
- Teach Staff about the importance of OTT
- Instruct and inform patients, emphasizing the importance of daily treatment
- Prescribe non only total dose and fractionation but also OTT
- Start curative treatment on a Monday
- Never finish treatment on a Monday (last fraction on a Saturday or treat twice on a Friday
- Document the causes of interruptions



Active measures recommended to maintain the prescribed OTT (2)

- Plan some large planned interruptions and Plan monthly machine maintenance
- Plan changes of technique with sufficient warning to satisfy internal organization
- Plan to transfer patients to a second machine if there are unavoidable long gaps
- Do not recommend routine breaks for acute reactions. Develop homogeneous criteria for the prescription of breaks for acute toxicity
- Offer psychosocial and nursing support to prevent toxicity. Use proper medication and local measures. Plan dental extraction before treatment. Place feeding tubes in appropriate patients.
- Compensate for short gaps of one day by treating the patient at the weekend or twice on the day after the gap
- Report realized OTT, causes of interruptions and methods for counteracting or compensating for the gap.

Unplanned interruptions in RT?



Associazione Italiana
Radioterapia e Oncologia clinica

SurveyMonkey®

maggio e giugno 2022

Survey interruzioni trattamenti radioterapici

(rivolta a tutti i Direttori/Responsabili Centri di Radioterapia italiani)

Unpublished data

Survey interruzioni trattamenti radioterapici

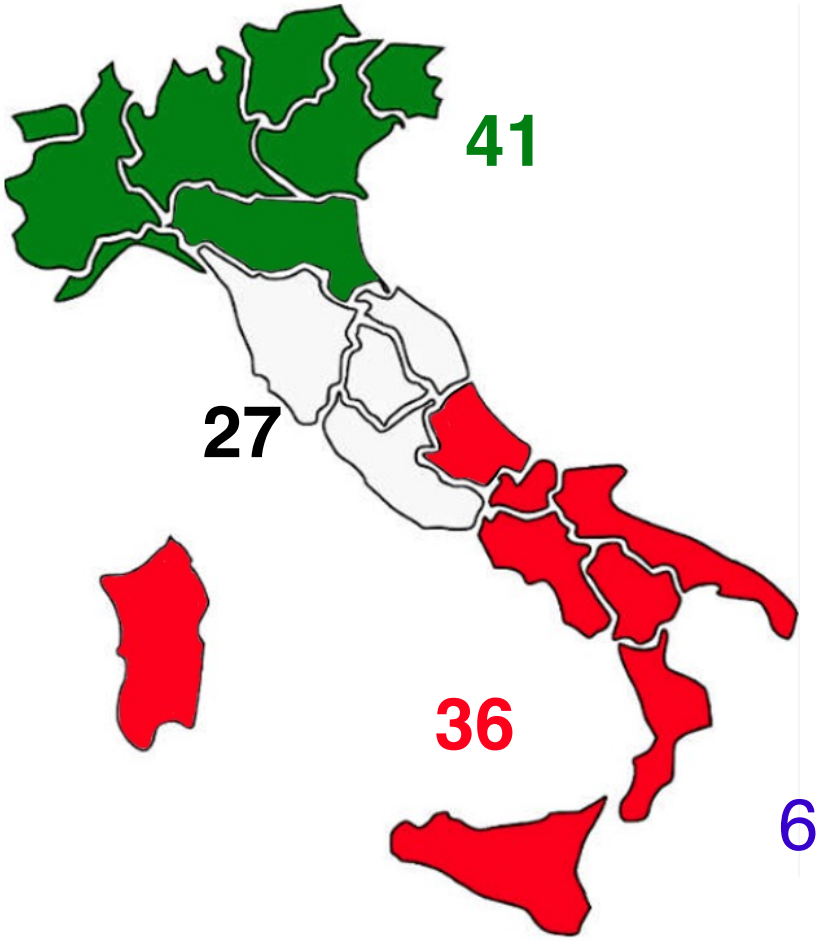
(rivolta a tutti i Direttori/Responsabili Centri di Radioterapia italiani)

- General informations
- Radiobiological knowledge
- Procedures followed

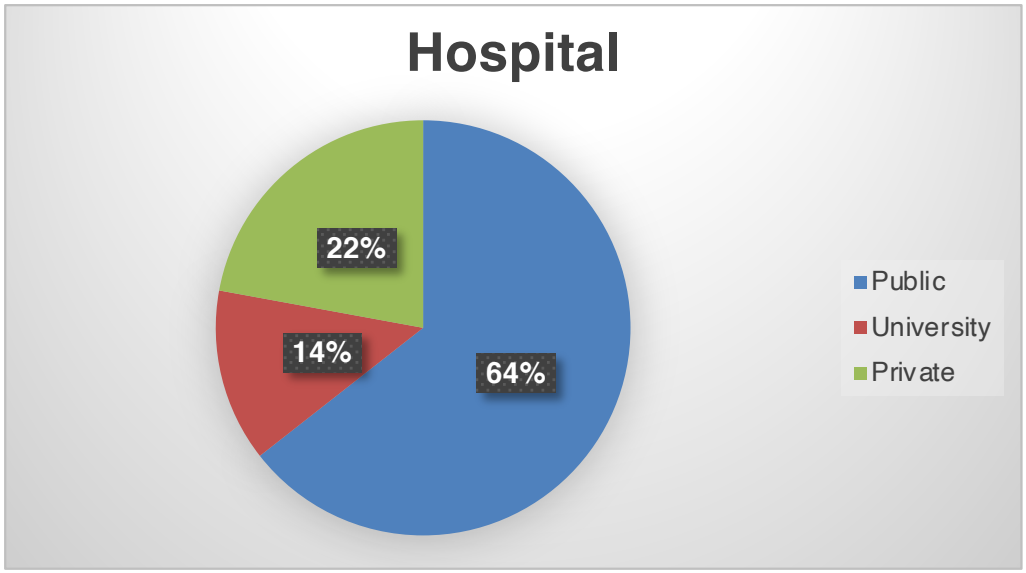
Survey interruzioni trattamenti radioterapici

(rivolta a tutti i Direttori/Responsabili Centri di Radioterapia italiani)

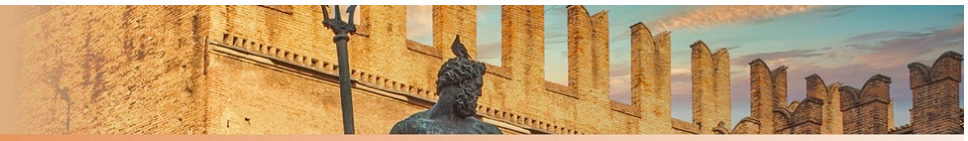
- General informations
- Radiobiological knowledge
- Procedures followed



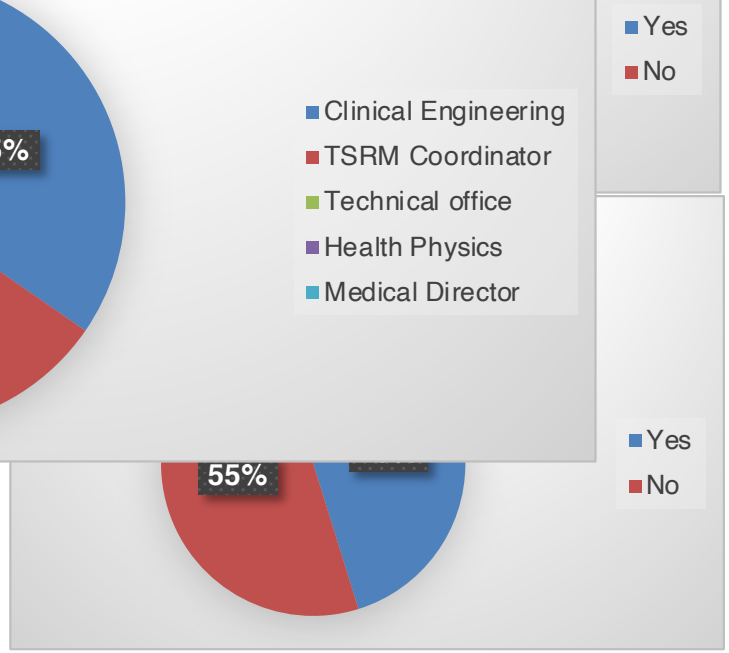
104 answers (56,8%)



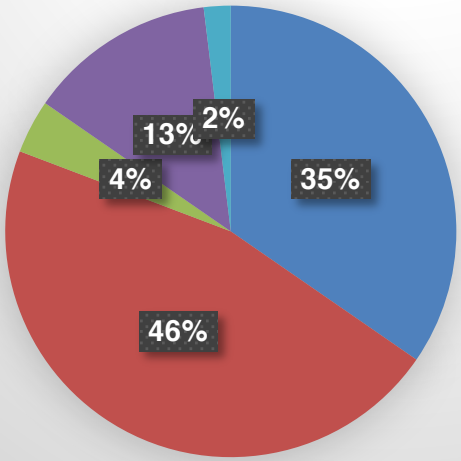
64 ♂ 40 ♀ median age: 57 y (34-74)



Have you been appointed responsible for the linac

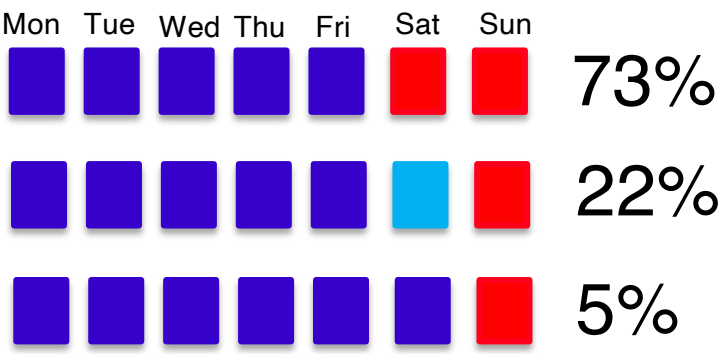


In the center where you work, who manages Linac breakdowns?



17 RT centers has only 1 Linac

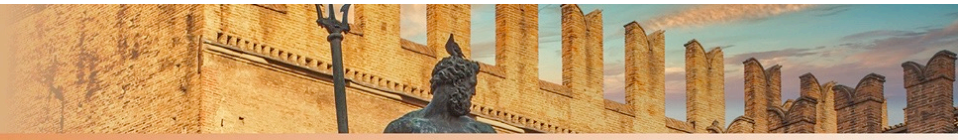
Activity



Survey interruzioni trattamenti radioterapici

(rivolta a tutti i Direttori/Responsabili Centri di Radioterapia italiani)

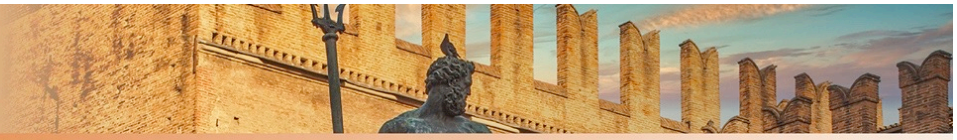
- General informations
- Radiobiological knowledge
- Procedures followed



Survey interruzioni trattamenti radioterapici

(rivolta a tutti i Direttori/Responsabili Centri di Radioterapia italiani)

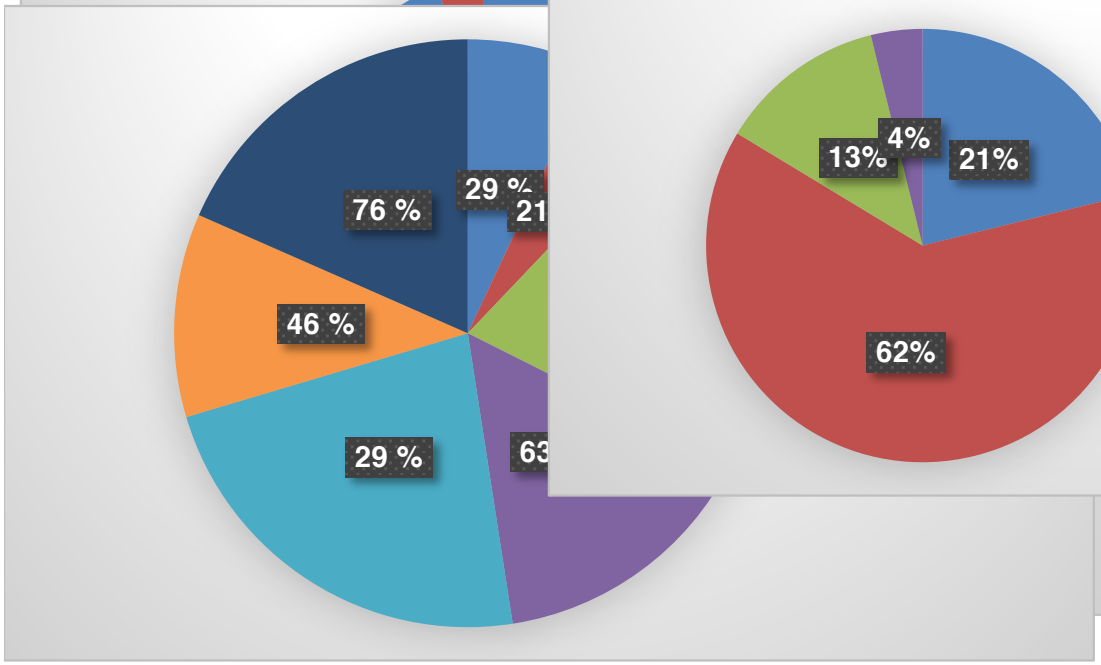
- General informations
- Radiobiological knowledge
- Procedures followed



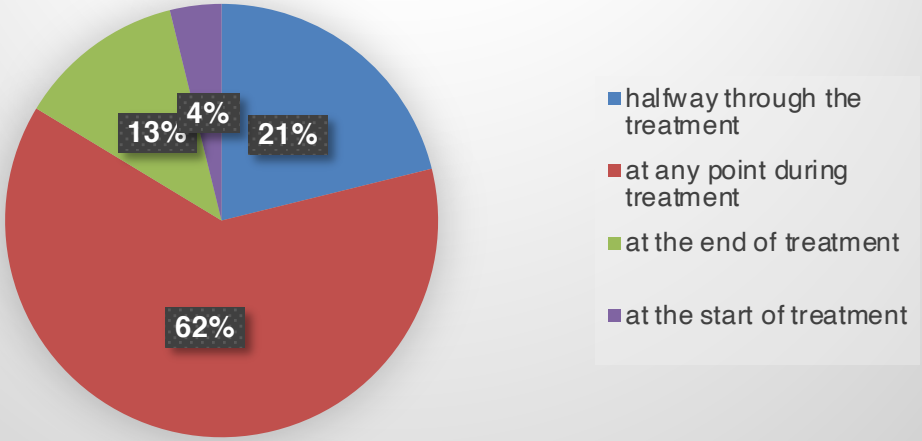
Are interruptions
to mar

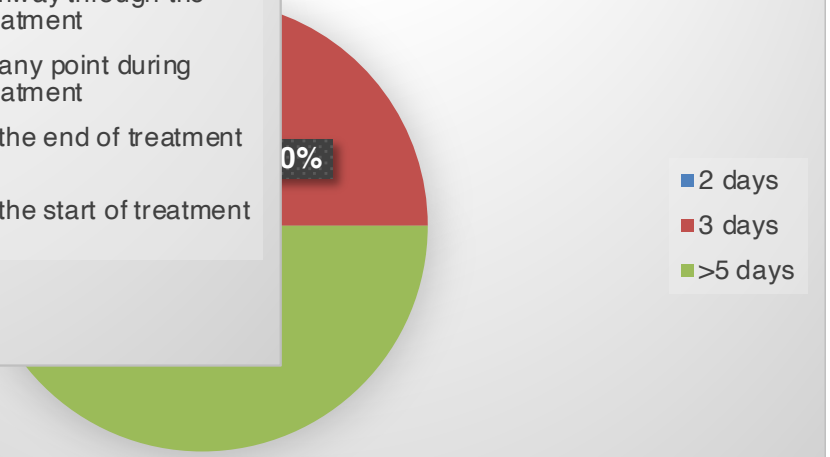
a critical issue
age?

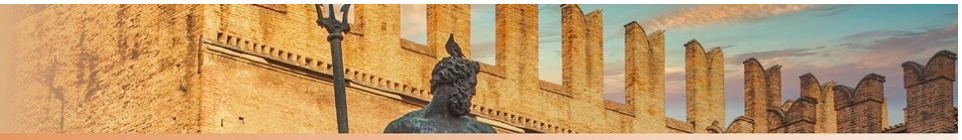
off RT treatment
itical?



At what stage of the treatment do you believe that the interruption could have a negative impact on the outcome?







Survey interruzioni trattamenti radioterapici

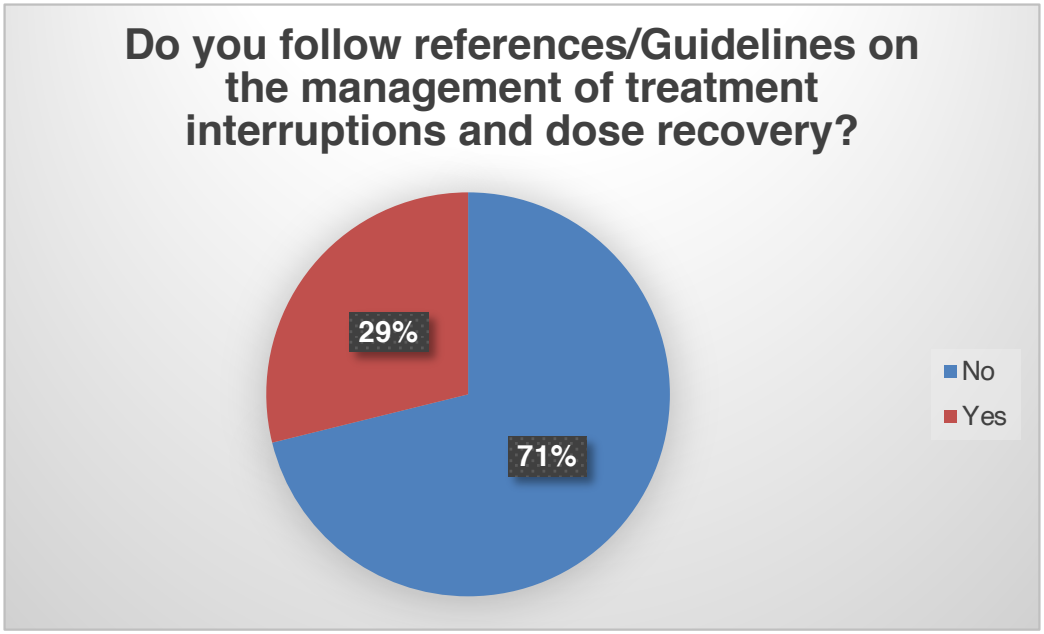
(rivolta a tutti i Direttori/Responsabili Centri di Radioterapia italiani)

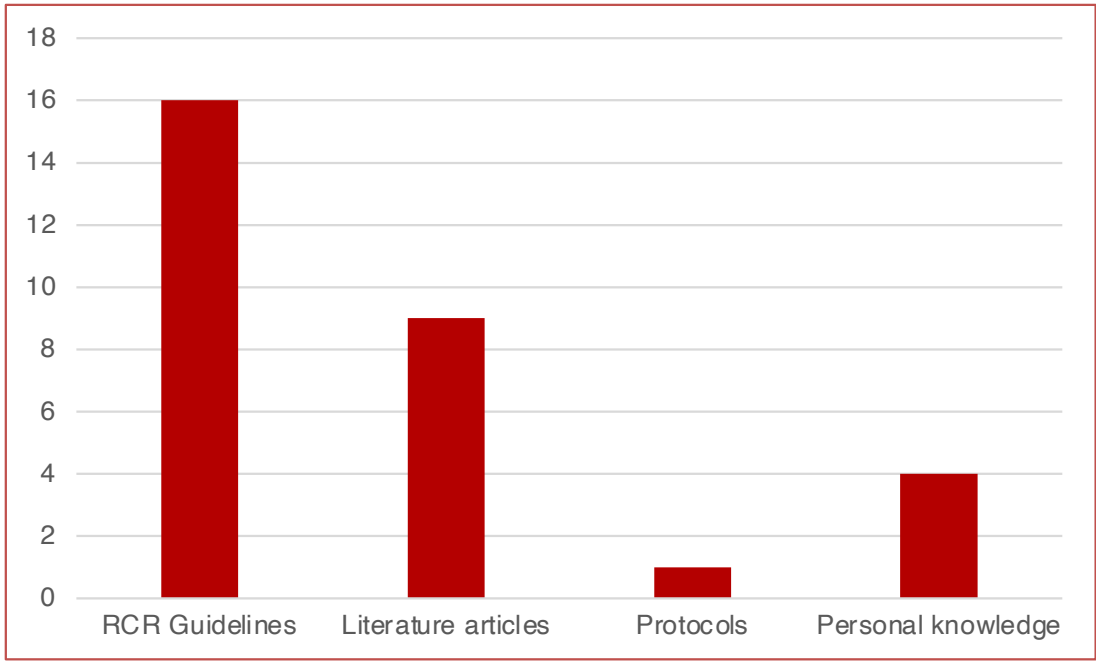
- General informations
- Radiobiological knowledge
- Procedures followed

Survey interruzioni trattamenti radioterapici

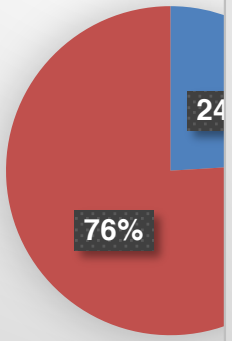
(rivolta a tutti i Direttori/Responsabili Centri di Radioterapia italiani)

- General informations
- Radiobiological knowledge
- Procedures followed


Do you follow references/Guidelines on the management of treatment interruptions and dose recovery?
29%
71%
No
Yes

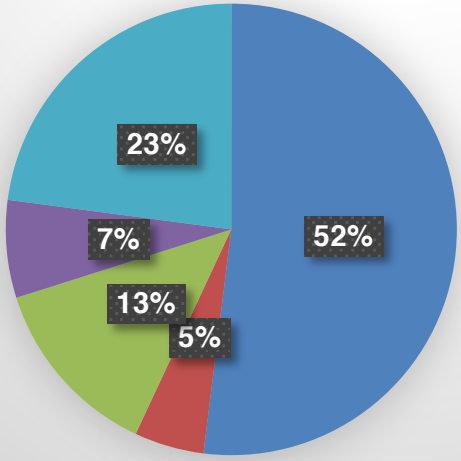

18
16
14
12
10
8
6
4
2
0
RCR Guidelines
Literature articles
Protocols
Personal knowledge

Is there a written procedure for dealing with treatment interruptions at the center where yo



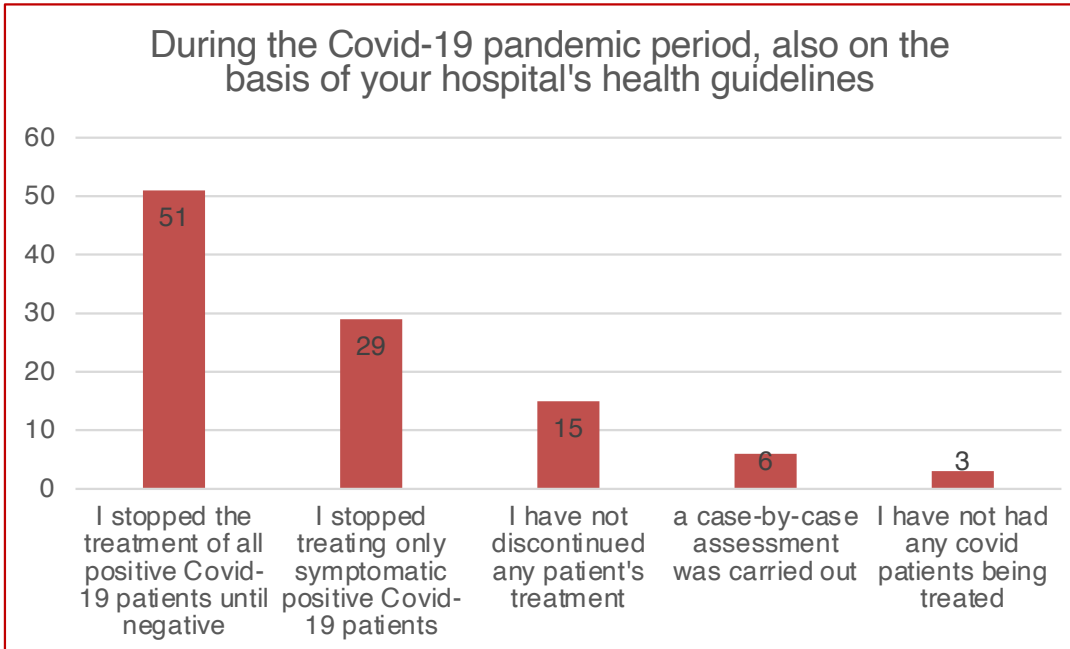
In the center where you work, are interruptions in treatment of patients monitored?

Reason for discontinuation of RT treatment

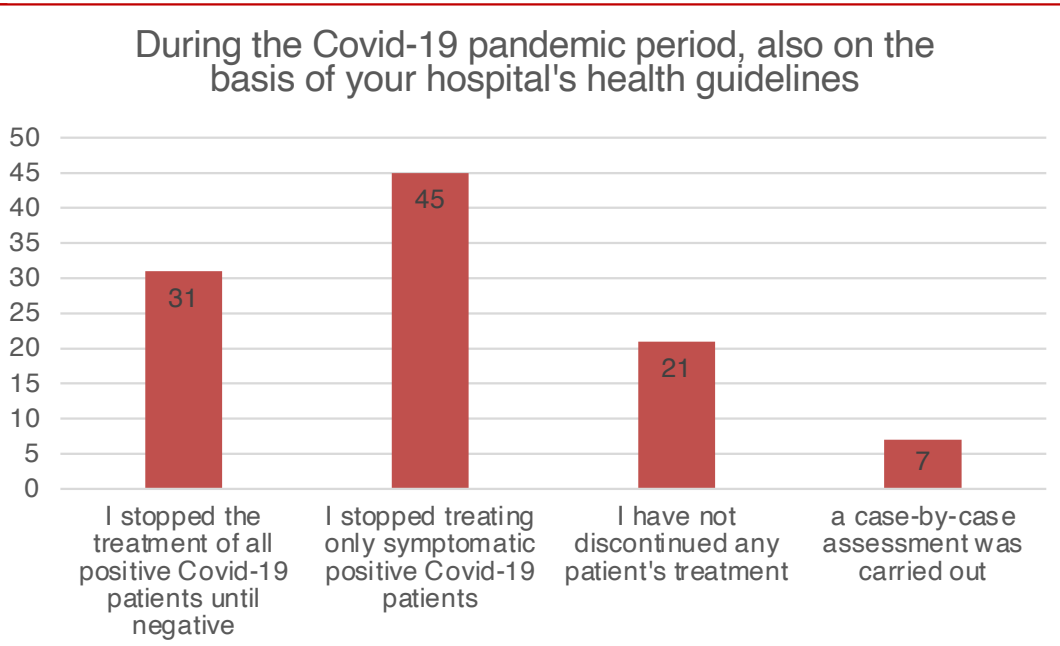


Covid 19 and unplanned interruptions in RT

Before the advent of vaccines

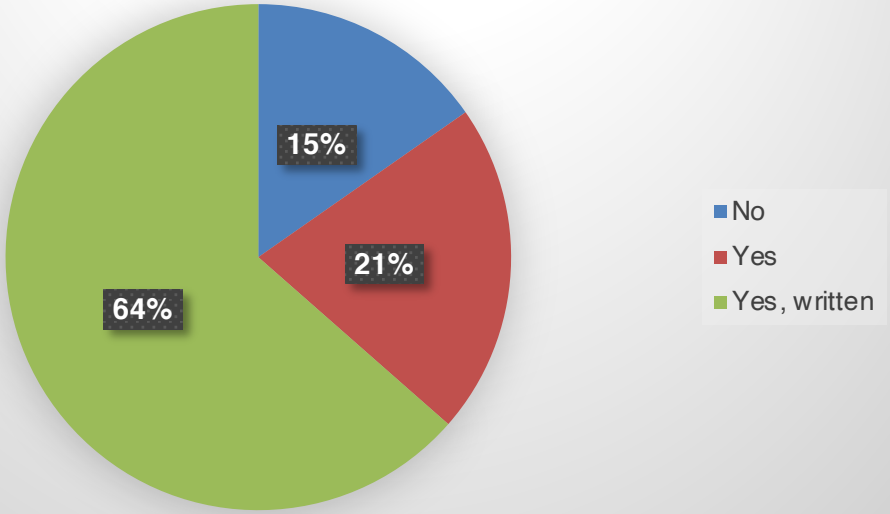


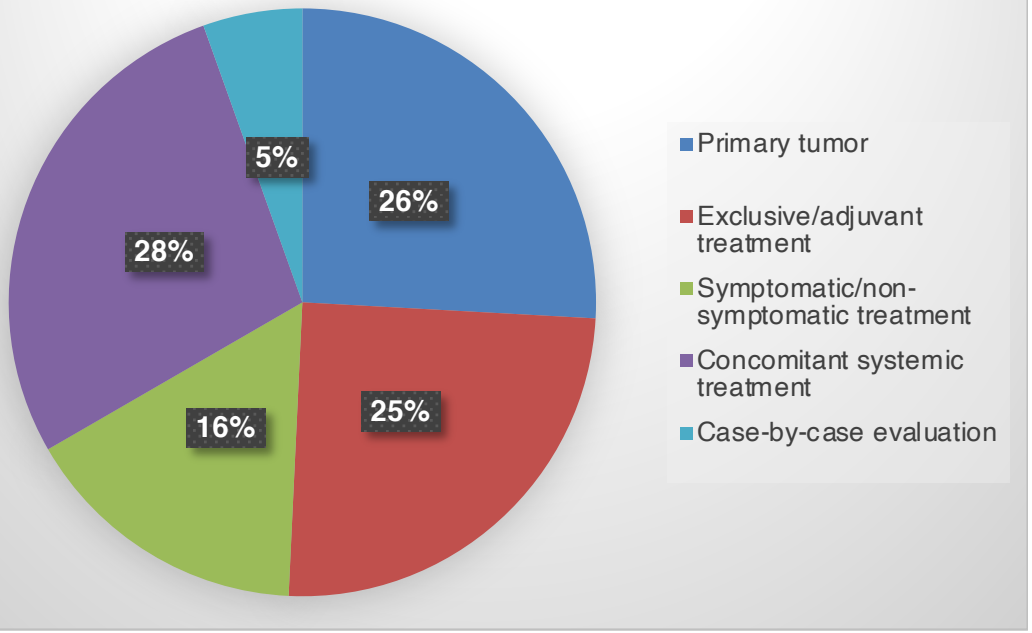
After the advent of vaccines



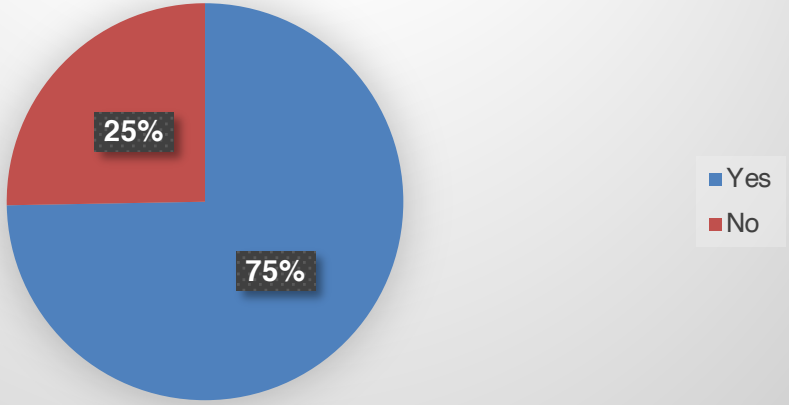
In case of breakdown linac move the patients to other linacs?

Do you follow procedures?

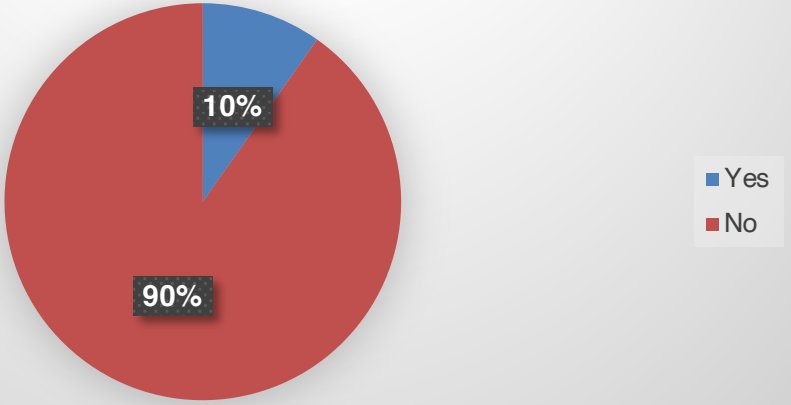




Do you recalculate the treatment plan before moving the patient to the other linac?

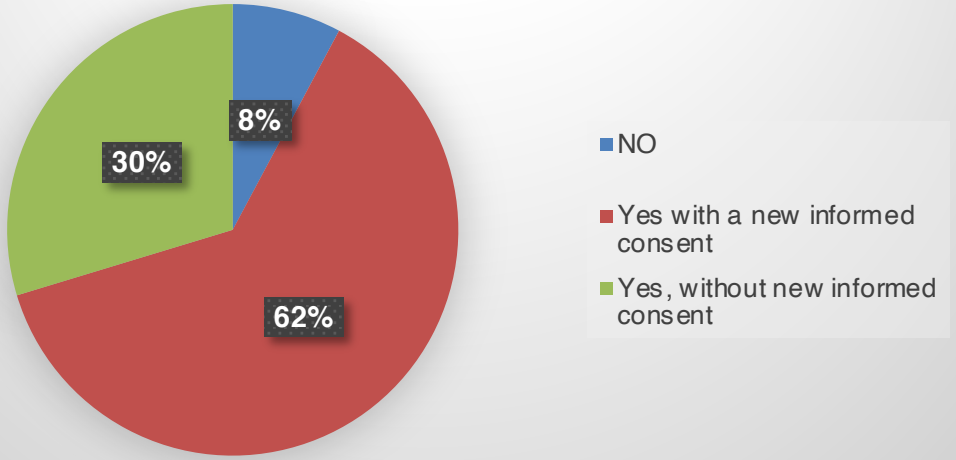


Do you calculate the treatment plan for two different linacs before starting the treatment?

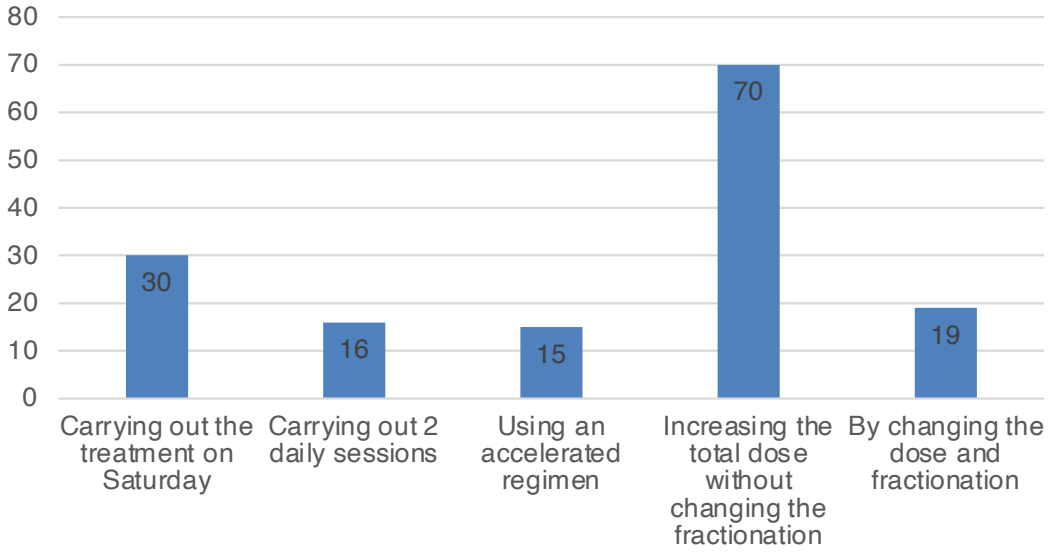


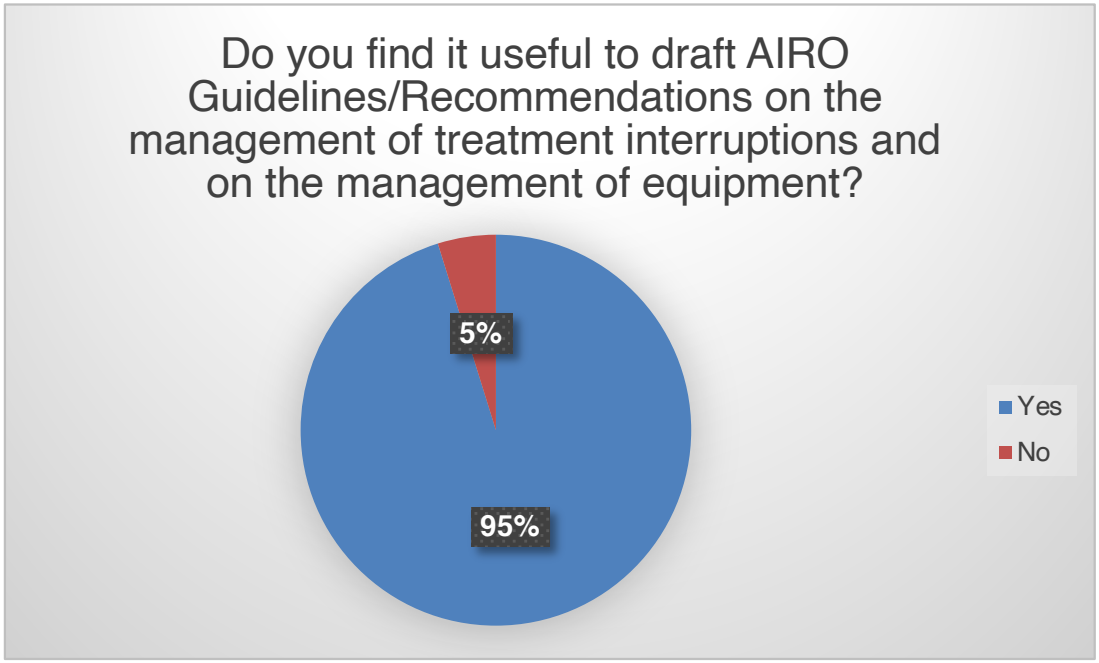
In the center where you work, is there a recovery of the dose not administered following interruptions?

If you change the fractionation, do you inform the patient?



How do you recover the dose?




Do you find it useful to draft AIRO Guidelines/Recommendations on the management of treatment interruptions and on the management of equipment?
5%
95%
Yes
No