LINFOMI PRIMITIVI CUTANEI DI DERIVAZIONE T-LINFOCITARIA:

la multidisciplinarità ottimizza il risultato

29 OTTOBRE 2021

NAPOLI Hotel Royal Continental

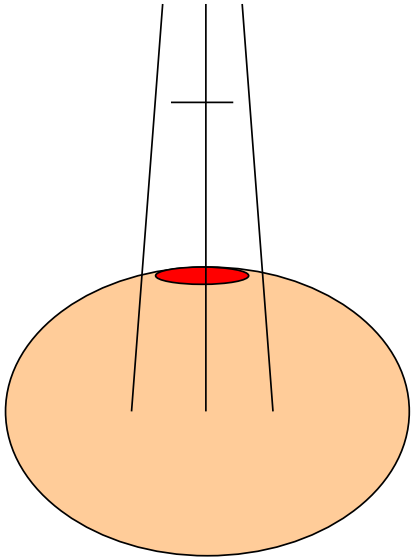
Il ruolo del Radioterapista

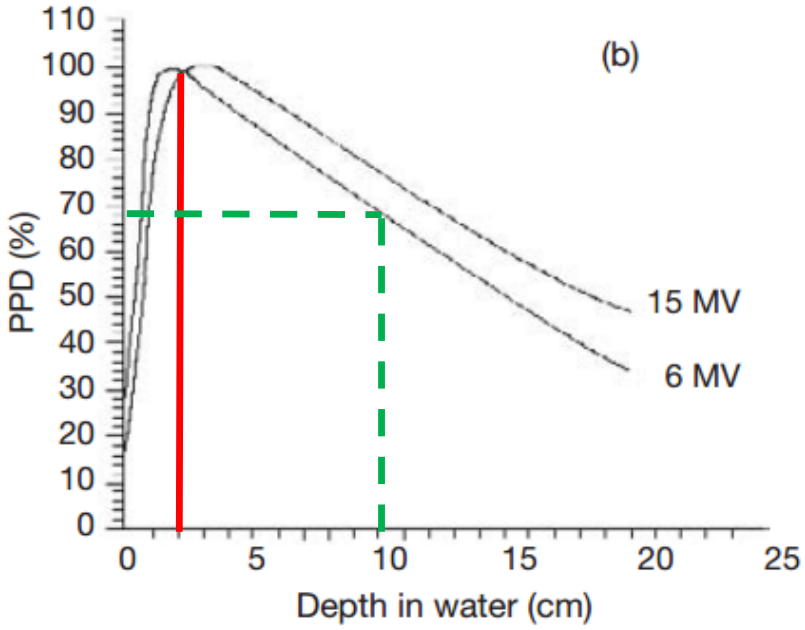
Dr *G. Simontacchi*
SOD Radioterapia
AOU Careggi - Firenze

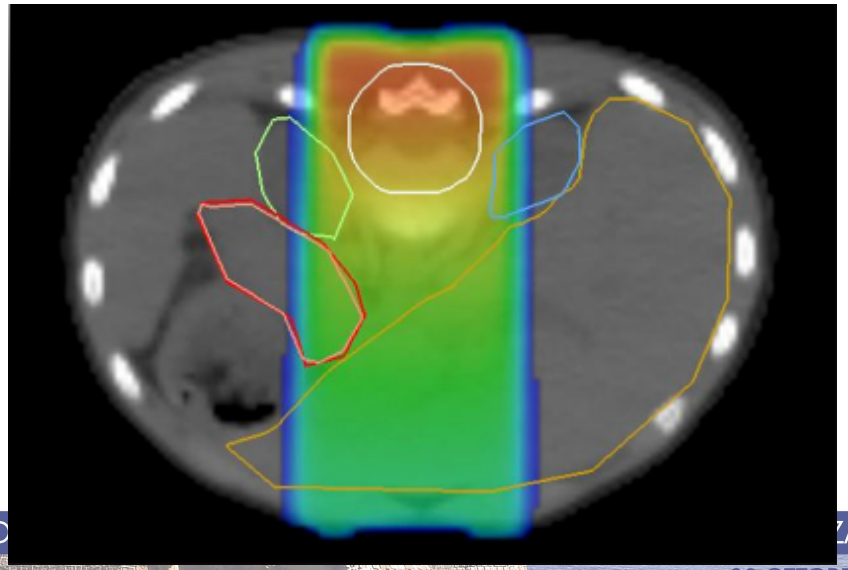
RADIOTERAPIA NEI LINFOMI CUTANEI

- Scopo di ogni trattamento medico è quello di ottenere l'obiettivo terapeutico con la minima tossicità
- Per la radioterapia: erogare una dose precisa di radiazioni ad un volume bersaglio ben definito con il minimo danno ai tessuti circostanti
- Come ottenere questo risultato quando il volume "target" è la cute?
- E' possibile farlo anche quando il "target" è l'intera superficie corporea?

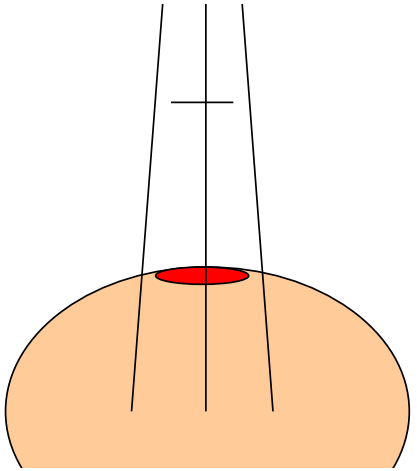
RADIOTERAPIA CON FASCIO DI FOTONI

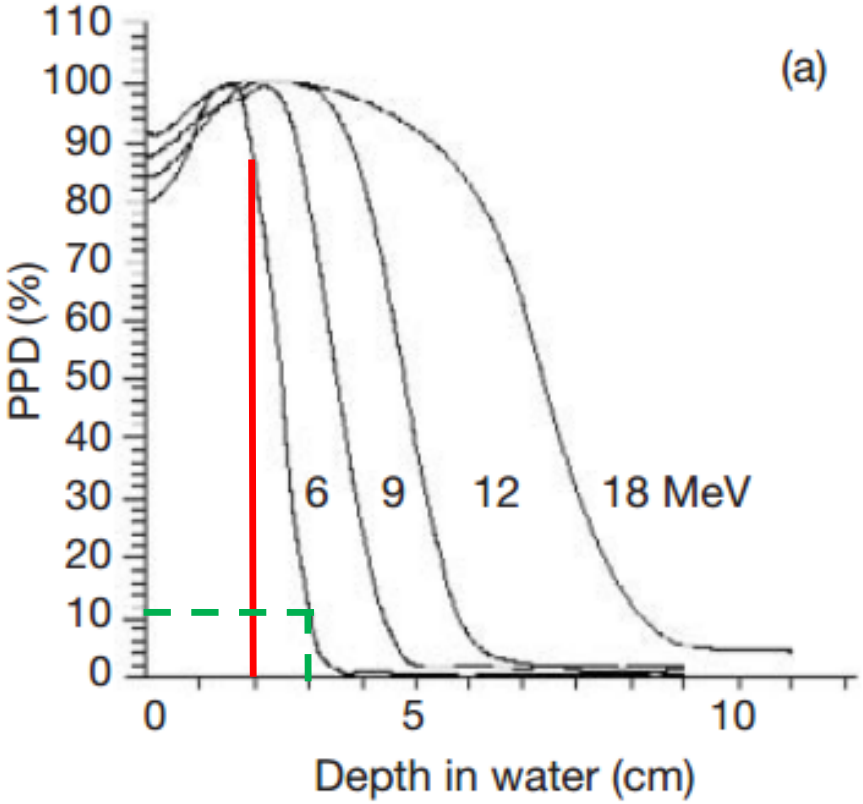


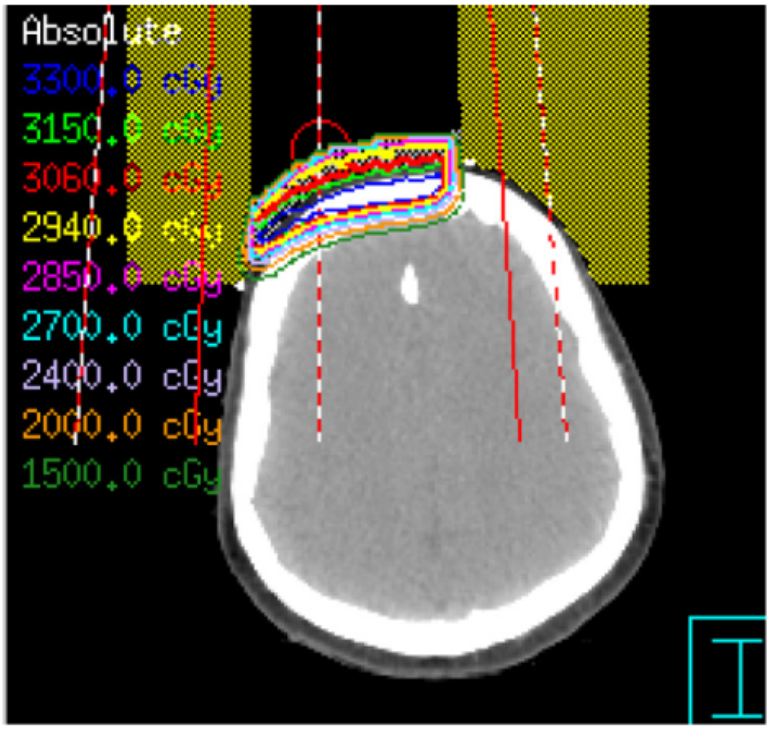




RADIOTERAPIA CON FASCIO DI ELETTRONI







TOLERANCE OF NORMAL TISSUE TO THERAPEUTIC IRRADIATION

B. EMAMI, M.D.,[1] J. LYMAN, PH.D.,[5] A. BROWN, M.D.,[4] L. COIA, M.D.,[3] M. GOITEIN, PH.D.,[4]
J. E. MUNZENRIDER, M.D.,[4] B. SHANK, M.D.,[2] L. J. SOLIN, M.D.[3] AND M. WESSON, M.D.[2]

Organ	TD 5/5 Volume			TD 50/5 Volume			Selected endpoint
	1/3	2/3	3/3	1/3	2/3	3/3	
Kidney I	5000	3000*	2300	—	4000*	2800	Clinical nephritis
Kidney II							
Bladder	N/A	8000	6500	N/A	8500	8000	Symptomatic bladder contracture and volume loss
Bone:							
Femoral Head I and II	—	—	5200	—	—	6500	Necrosis
T-M joint mandible	6500	6000	6000	7700	7200	7200	Marked limitation of joint function
Rib cage	5000	—	—	6500	—	—	Pathologic fracture
Skin	10 cm² / —	30 cm² / —	100 cm² / 5000	10 cm² / —	30 cm² / —	100 cm² / 6500	Telangiectasia
	7000	6000	5500	—	—	7000	Necrosis Ulceration
Brain	6000	5000	4500	7500	6500	6000	Necrosis Infarction
Brain stem	6000	5300	5000	—	—	6500	Necrosis Infarction
Optic nerve I & II	No partial volume		5000	—	—	6500	Blindness
Chiasma	No partial volume		5000	No partial volume		6500	Blindness
Spinal cord	5 cm / 5000	10 cm / 5000	20 cm / 4700	5 cm / 7000	10 cm / 7000	20 cm / —	Myelitis necrosis

Guidelines

Modern Radiation Therapy for Primary Cutaneous Lymphomas: Field and Dose Guidelines From the International Lymphoma Radiation Oncology Group

Lena Specht, MD, PhD,* Bouthaina Dabaja, MD,† Tim Illidge, MD, PhD,‡ Lynn D. Wilson, MD,§ and Richard T. Hoppe, MD||, on behalf of the International Lymphoma Radiation Oncology Group

Mycosis fungoides – Total Skin Irradiation

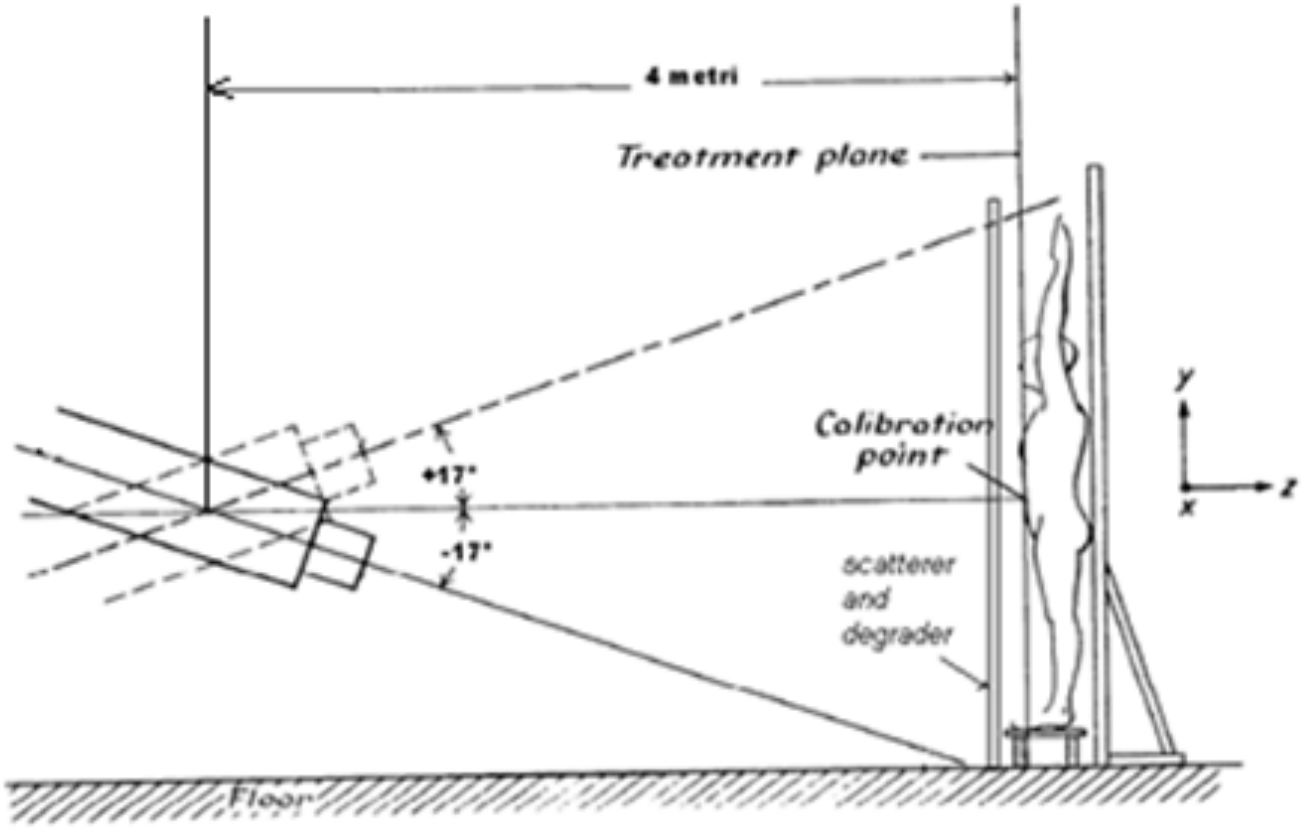


Figura 1 Schema della configurazione di trattamento per TSET.

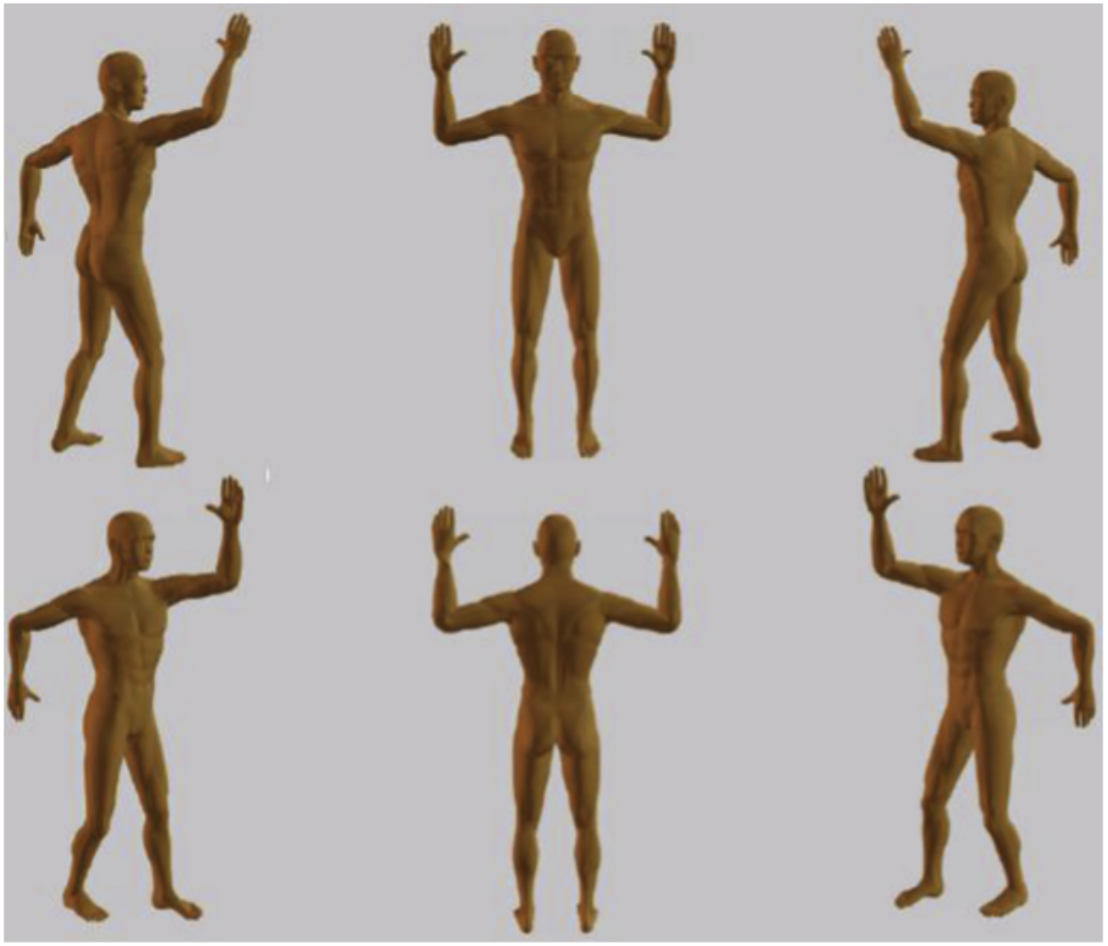
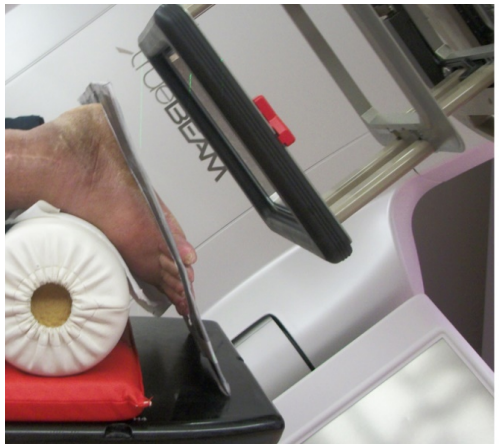
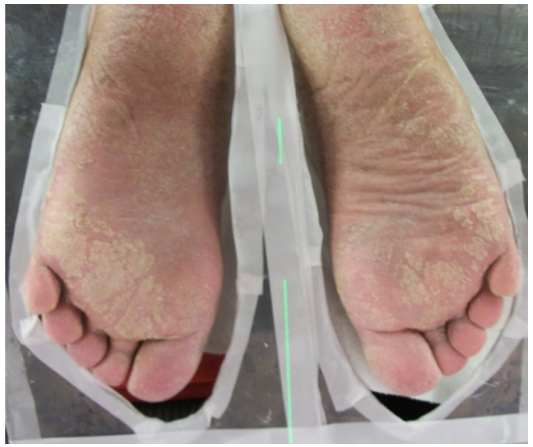


Fig. 10. Patient positions for total skin electron beam therapy, 6-field technique. The straight anterior, right posterior oblique, and left posterior oblique fields are treated on one day. The straight posterior, right anterior oblique, and left anterior oblique fields are treated the next day.

Regional patch treatments

-Scalp
-Axilla
-Skin under breasts
-Pannicular skin
-Groin/inner thighs
-Buttocks
-Perineal skin
-Soles





➢Aim of this technique is treating the **whole body surface** at a **limited depth** and with a **uniform dose** using an electron beam

-36Gy; 1Gy/die, 4days/week, 9 weeks ***(Stanford)***

-36Gy; 1,5Gy/die, 3days/week, 8 weeks ***(Heumann, 2014)***

-30Gy; 2Gy/die, 4days/week, 4 weeks ***(Ysebaert 2004)***

-35Gy; 1,16Gy/die, 5days/week, 6 weeks ***(Jones 2002)***

-24Gy; 3Gy/die, 3days/week, 4 weeks ***(Maingon 2000)***

STUDY

The Stanford University Experience With Conventional-Dose, Total Skin Electron-Beam Therapy in the Treatment of Generalized Patch or Plaque (T2) and Tumor (T3) Mycosis Fungoides

Daniel Navi, MD; Nadeem Riaz, MD; Yakir S. Levin, MD, PhD; Naomi C. Sullivan, BS; Youn H. Kim, MD; Richard T. Hoppe, MD

Table 1. Clinical Response and Outcomes of Cohort

Type of Therapy (No. of Patients	Median Follow-up, y	No. (%)		Median , y		
		CCR	PR	OS,	PFS	FFR
T2 class						
27 Received TSEBT monotherapy	13.0	41 (72)	16 (28)	11.3	8.9	2.4
43 Received TSEBT + HN2	8.9	33 (77)	10 (23)	10.9	8.5	2.7
Total of 103 patients with T2 disease[a]	11.7	77 (75)	26 (25)	10.9	8.5	2.4
T3 class						
27 Received TSEBT monotherapy	5.5	12 (44)	15 (56)	4.2	1.8	1.0
42 Received TSEBT + HN2	4.6	20 (48)	22 (52)	3.9	2.9	0.8
Total of 77 patients with T3 disease[a]	5.2	36 (47)	41 (53)	4.7	2.9	0.8

ORR 100% - CR 63%

EFFETTI COLLATERALI ACUTI E SUBACUTI

- Eritema
- Desquamazione umida
- Flittene (++ piedi)
- Fatigue
- Alterazioni ungueali (fino alla caduta)
- Edema mani e piedi
- Epistassi
- Ginecomastia temporanea
- Parotite transitoria
- Alopecia
- Iperpigmentazione cutanea
- Ipoidrosi

EFFETTI COLLATERALI CRONICI

- Atrofia cutanea
- Alopecia permanente
- Distrofia ungueale
- Infertilità nell'uomo

REVISITING LOW-DOSE TOTAL SKIN ELECTRON BEAM THERAPY IN MYCOSIS FUNGOIDES

CAMERON HARRISON, M.D.,* JAMES YOUNG, D.O.,* DANIEL NAVI, M.D.,* NADEEM RIAZ, M.D.,†
BHARATHI LINGALA,* YOUN KIM, M.D.,* AND RICHARD HOPPE, M.D.†

*Department of Dermatology and †Department of Radiation Oncology, Stanford Cancer Center, Stanford, California

Table 1. Initial course clinical response by dose

		No. of patients/total (%) per dose group			
T class or range	Response	5–<10 Gy	10–<20 Gy	20–<30 Gy	5–<30 Gy
T2	CR	1/7 (14)	13/25 (52)	7/19 (37)	21/51 (41)
	PR	5/7 (71)	11/25 (44)	12/19 (63)	28/51 (55)
	OR	6/7 (85)	24/25 (96)	19/19 (100)	49/51 (96)
T3	CR	2/8 (25)	1/14 (7)	2/7 (29)	5/29 (17)
	PR	5/8 (63)	13/14 (93)	5/7 (71)	23/29 (79)
	OR	7/8 (88)	14/14 (100)	7/7 (100)	28/29 (96)
T4	CR	0/4 (0)	4/12 (33)	2/6 (33)	6/22 (27)
	PR	4/4 (100)	8/12 (67)	3/6 (50)	15/22 (68)
	OR	4/4 (100)	12/12 (100)	5/6 (83)	21/22 (95)
T2–T4	CR	3/19 (16)	18/51 (35)	11/32 (34)	32/102 (31)
	PR	14/19 (74)	32/51 (63)	20/32 (63)	66/102 (65)
	OR	17/19 (90)	50/51 (98)	31/32 (97)	98/102 (96)

Abbreviations: CR = complete response (clinical resolution of all cutaneous lesions); PR = partial response (>50% resolution of cutaneous lesions defined by the physicians global assessment); OR = Overall response (PR plus CR).

Low-dose total skin electron beam therapy as an effective modality to reduce disease burden in patients with mycosis fungoides: Results of a pooled analysis from 3 phase-II clinical trials

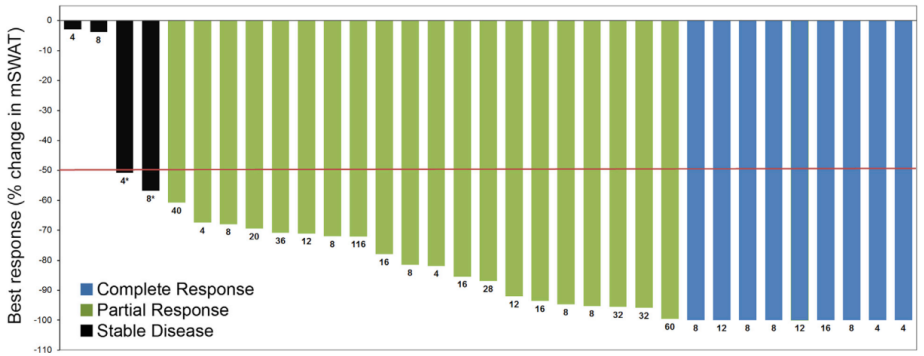
Richard T. Hoppe, MD,[a] Cameron Harrison, MD,[b] Mahkam Tavallaee, MD, MPH,[b] Sameer Bashey, MD,[b] Uma Sundram, MD, PhD,[b,c] Shufeng Li, MS,[b] Lynn Million, MD,[a] Bouthaina Dabaja, MD,[d] Pamela Gangar, MD,[e] Madeleine Duvic, MD,[e] and Youn H. Kim, MD[b]
Stanford, California, and Houston, Texas

Table II. Best overall response to treatment at study termination, total time to response, and duration of clinical response

Characteristic	n (%)	Response data CR	PR	SD	PD	ORR n (%)
Clinical stage						
All	33 (100)	9 (27)	20 (61)	4 (12)	0	29 (88)
IB	22 (67)	7	13	2	0	20 (91)
IIA	2 (6)	0	2	0	0	2 (100)
IIB	7 (21)	2	4	1	0	6 (96)
IIIA	2 (6)	0	1	1	0	1 (50)
Median time to response (range)		7.6 (3-12.4) wk				
Median duration of clinical benefit (95% CI)		70.7 (41.8-133.8) wk				

CI, Confidence interval; *CR*, complete response; *PD*, progressive disease; *PR*, partial response *SD*, stable disease.

33 pts; 12 Gy, 1 Gy per fraction over 3 weeks



J Am Acad Dermatol, 2014

Low-Dose (10-Gy) Total Skin Electron Beam Therapy for Cutaneous T-Cell Lymphoma: An Open Clinical Study and Pooled Data Analysis

Maria R. Kamstrup, PhD, MD,* Robert Gniadecki, DMSc, PhD, MD,* Lars Iversen, DMSc, MD,† Lone Skov, DMSc, PhD, MD,‡ Peter Meidahl Petersen, DMSc, PhD, MD,§ Annika Loft, DMSc, MD,|| and Lena Specht, DMSc, MD§

21 pts
10 Gy, 1 Gy per fraction,
4 fractions per week

RESULTS:

- ORR 95%
- CR 29%; VGPR 29%

- Complete cutaneous response (CR+VGPR)
  - T2: 66%
  - T3: 60%
  - T4: 25%

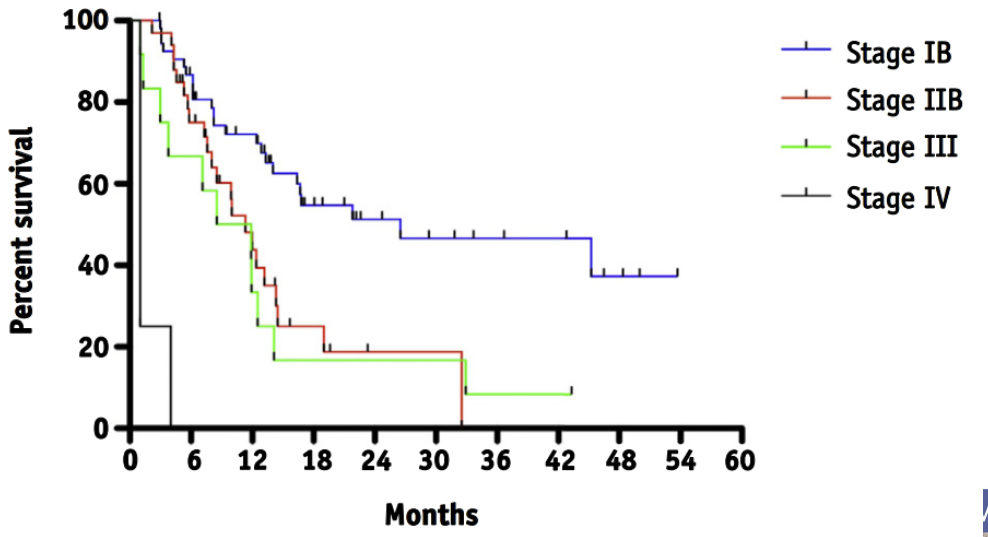
TOXICITY (only G1-G2):

- transient total or partial alopecia 35%
- skin discomfort 25%
- superficial ulcerations and blisters 15%
- xerosis 15%
- ocular irritation 15%
- erythema 10%
- nail changes 10%
- hyperpigmentation 10%
- hypohidrosis 5%
- localized ankle edema 5%
- mouth dryness 5%

IJROBP, 2015

The Results of Low-Dose Total Skin Electron Beam Radiation Therapy (TSEB) in Patients With Mycosis Fungoides From the UK Cutaneous Lymphoma Group

Stephen Morris, MBBS, MRCP, FRCR,* Julia Scarisbrick, MBChB, FRCP, MD,† John Frew, MBChB, MRCP, FRCR,‡ Clive Irwin,† Robert Grieve, FRCP, FRCR,† Caroline Humber, MRCP, FRCR,† Aleksandra Kuciejewska, MRCP,* Sally Bayne, DCR (T),* Sophie Weatherhead, MBBS, BSc, MRCP, PhD,‡ Fiona Child, MD, MRCP,* Mary Wain, MD, MRCP,* and Sean Whittaker, MD, FRCP*



- 103 pts.
- ORR 87% (95% in IB-IIB pts.)
- CR 18% (21% in IB-IIB pts.)
- Median DOCB 12,2m (16,8m in IB pts.)

IJROBP, 2017

Mycosis fungoides - Low-Dose TSEBI

Advantages:

- Shorter treatment course
- Reduction of radiation-related toxicities
- Reduction of treatment costs (time consuming!)
- Reduced cost for the patients
- Improved patient compliance
- Possibility of re-treatment (multiple re-treatments!)
- Possibility to associate drugs (Radiosensitizers? Immunomodulators?)

Disadvantages:

- Lower CR rate
- Shorter duration of response

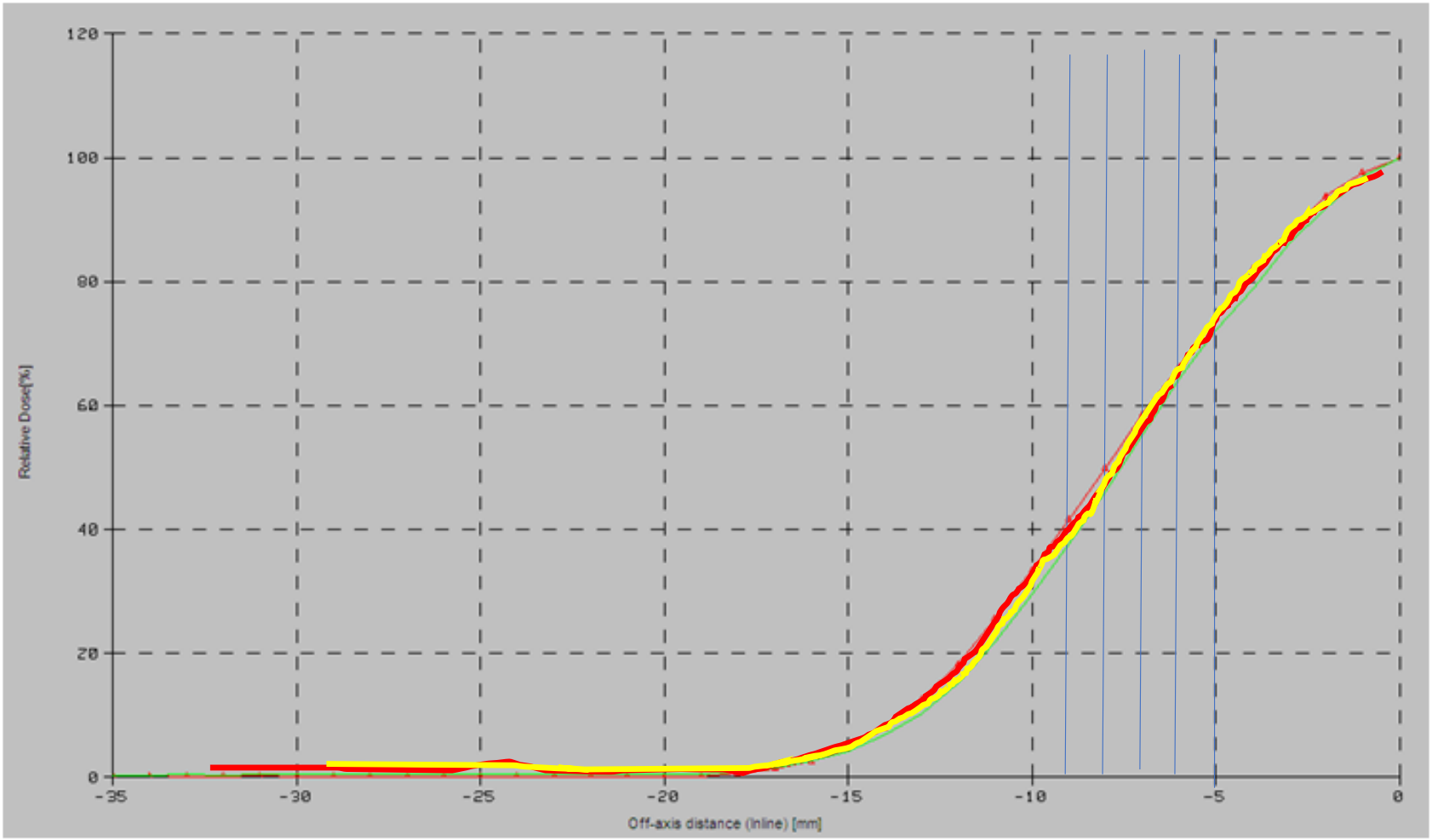


Figura 4 PDD per il fascio HDRE1 con gantry a 253° (curva rossa) e 287° (curva verde).

- Se la porzione profonda di una placca riceve il 60% della dose nominale di prescrizione…
  -Prescrizione 36Gy: dose ricevuta 21,6Gy
  -Prescrizione 10Gy: dose ricevuta 6Gy

- Se la porzione profonda di un nodulo riceve il 40% della dose nominale di prescrizione…
  -Prescrizione 36Gy: dose ricevuta 14,4Gy
  -Prescrizione 10Gy: dose ricevuta 4Gy

→ **«BOOST» pre-TSEBI**

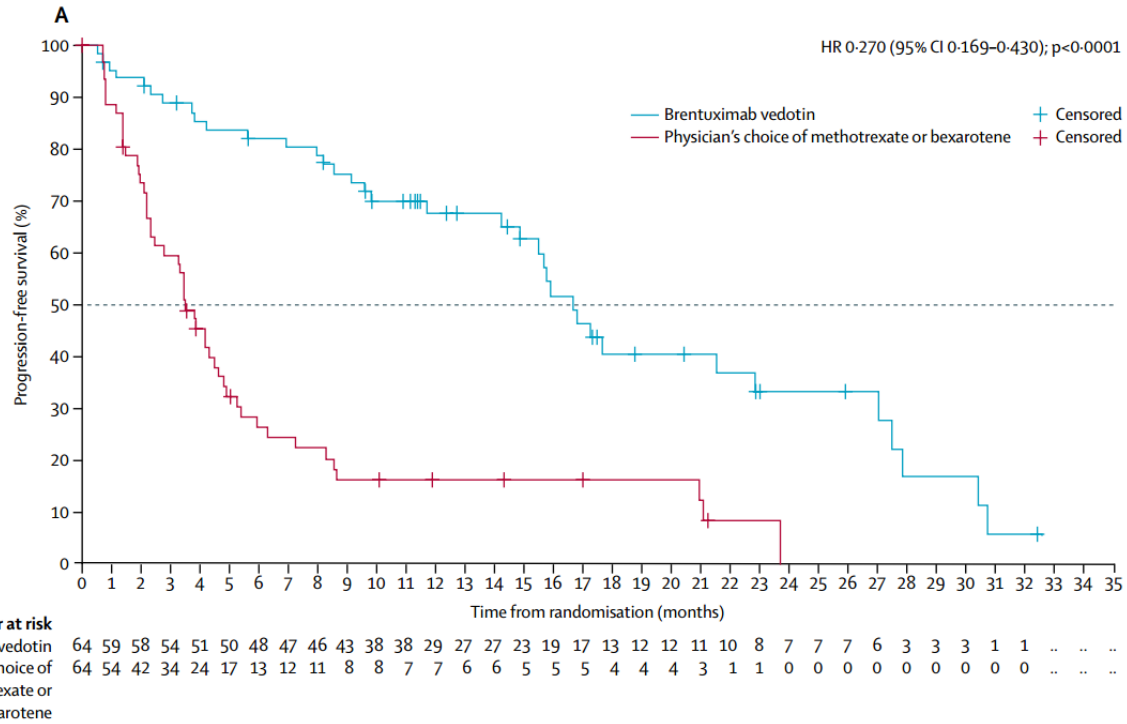
- 8Gy singola frazione
- 8Gy 4Gy/die
- 9-15Gy 3Gy/die
- 10-16Gy 2Gy/die


www.benheys.squarespace.com

Author	DRUG	N°	Results	Toxicity
Dummer 2012	LIPOSOMAL DOXORUBICIN	49	50,8% ORR, 6.1% CR	
Duvic 2001	BEXAROTENE	65	54% ORR (7% CR)	Headache 46%, Nausea 25%, Hiperlipemia 71%
Illidge 2013	GEMCITABINE+ BEXAROTENE	36	PR a 12 sett 25%, PFS 5.3 mesi, OS 21.2 mesi	
Pellegrini 2014	GEMCITABINE	25	OR 48%, CR 20% Median PFS 13,1m	Liver 40% G1-G2 (8% G3-G4) Hematol 68% G1-G2
Jidar 2009	GEMCITABINE	23	ORR 77,7%, CR 11,1%	Hematol 35% G1-2 28% G3-4 Infection 26% 26% treatment interr.
Duvic 2015	MOGAMULIZUMAB	22	ORR 28,6%, CR 4,8% Median PFS 11,4m	Nausea 31% (4,8% G3)
Foss 2016	ROMIDEPSIN	30	ORR 45-60% CR 10% TTP 8,3m	Nausea G1-2 56% >25% G3-4 AE
Prince 2017	BRENTUXIMAB VEDOTIN	131	ORR 65% CR 10%	29% SAE 24% discontinuations Neuropathy G1 25,7%; G2 31,8%; G3 9,1%

Brentuximab vedotin or physician's choice in CD30-positive cutaneous T-cell lymphoma (ALCANZA): an international, open-label, randomised, phase 3, multicentre trial

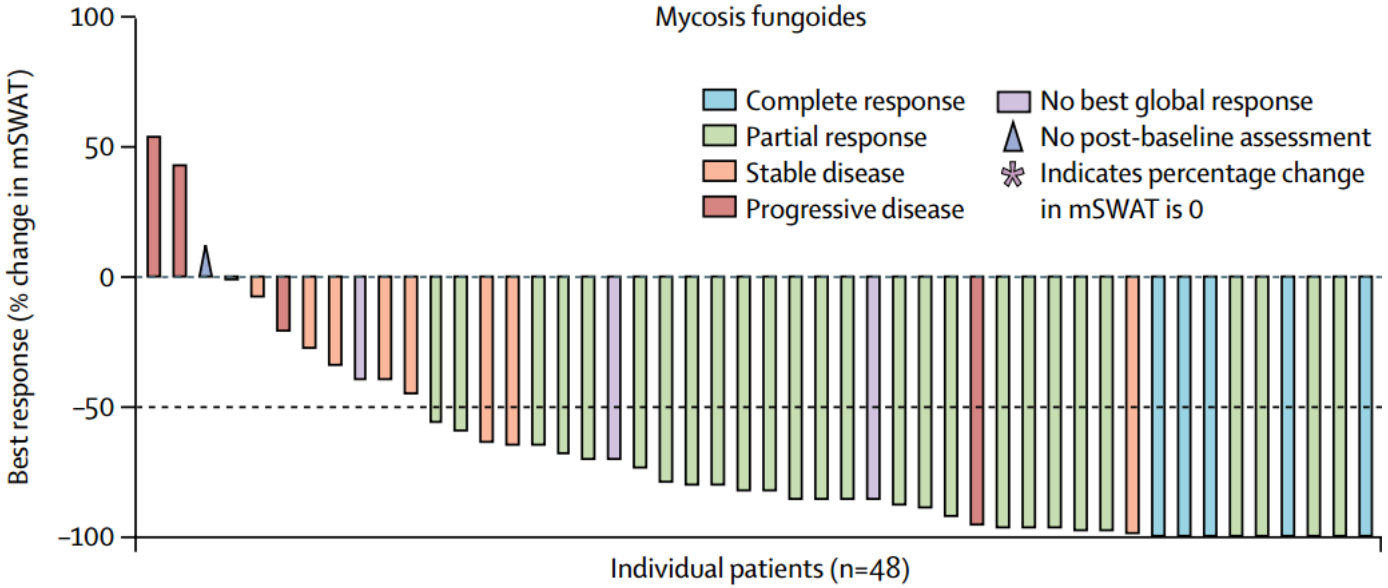
H Miles Prince, Youn H Kim*, Steven M Horwitz, Reinhard Dummer, Julia Scarisbrick, Pietro Quaglino, Pier Luigi Zinzani, Pascal Wolter, Jose A Sanches, Pablo L Ortiz-Romero, Oleg E Akilov, Larisa Geskin, Judith Trotman, Kerry Taylor, Stephane Dalle, Michael Weichenthal, Jan Walewski, David Fisher, Brigitte Dréno, Rudolf Stadler, Tatyana Feldman, Timothy M Kuzel, Yinghui Wang, Maria Corinna Palanca-Wessels, Erin Zagadailov, William L Trepicchio, Wenwen Zhang, Hui-Min Lin, Yi Liu, Dirk Huebner, Meredith Little, Sean Whittaker†, Madeleine Duvic†, on behalf of the ALCANZA study group‡*

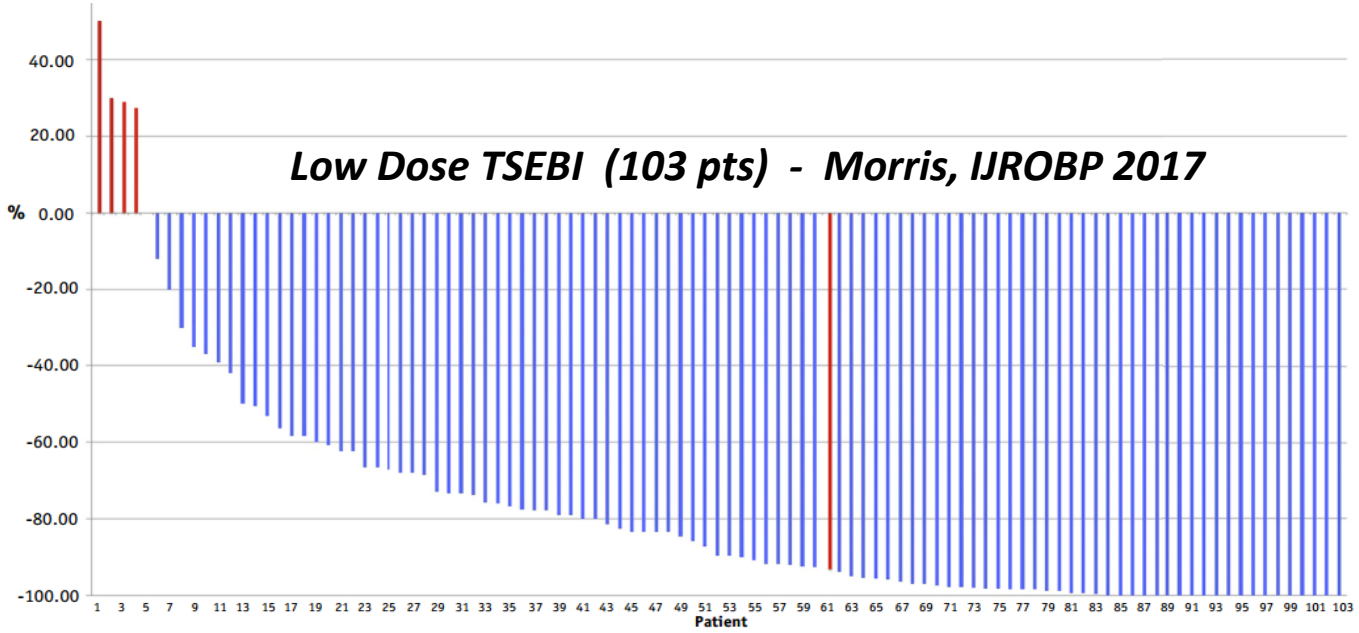


	Brentuximab vedotin				Physician's choice of methotrexate or bexarotene			
	Total (n=64)	ORR4	ORR	CR	Total (n=64)	ORR4	ORR	CR
ITT population	64 (100%)	36 (56%)*	43 (67%)	10 (16%)	64 (100%)	8 (13%)†	13 (20%)	1 (2%)
Mycosis fungoides	48 (75%)	24 (50%)	31 (65%)	5 (10%)	49 (77%)	5 (10%)	8 (16%)	0
Stage‡§								
IA–IIA	15 (31%)	6 (40%)	8 (53%)	1 (7%)	18 (37%)	4 (22%)	5 (28%)	0
IIB	19 (40%)	12 (63%)	13 (68%)	3 (16%)	19 (39%)	1 (5%)	3 (16%)	0
IIIA–IIIB	4 (8%)	2 (50%)	3 (75%)	0	2 (4%)	0	0	0
IVA	2 (4%)	2 (100%)	2 (100%)	1 (50%)	9 (18%)	0	0	0
IVB	7 (15%)	2 (29%)	4 (57%)	0	0	NA	NA	NA
pcALCL	16 (25%)	12 (75%)	12 (75%)	5 (31%)	15 (23%)	3 (20%)	5 (33%)	1 (7%)
Disease involvement‡								
Skin only	9 (56%)	8 (89%)	8 (89%)	4 (44%)	11 (73%)	3 (27%)	5 (45%)	1 (9%)
Extracutaneous disease	7 (44%)	4 (57%)	4 (57%)	1 (14%)	4 (27%)	0	0	0

Data are n (%). ORR4, ORR, and CR percentages are based on the number of patients in the total column. ORR4=achieved an objective response lasting at least 4 months. ORR=achieved an objective response. CR=achieved a complete response. ITT=intent to treat. NA=not applicable. pcALCL=primary cutaneous anaplastic large-cell lymphoma. *One patient with mycosis fungoides in the brentuximab vedotin group achieved a partial response after C1, C2, and C3, and discontinued because of an adverse event. About 4·3 months later the patient received chemotherapy (gemcitabine) before end-of-treatment visit. Total duration of response, including after receipt of gemcitabine, was 4·8 months. †One patient with pcALCL in the bexarotene group who achieved partial response after C2 and sustained it at C5 chose to withdraw from treatment. The patient received subsequent therapy (methotrexate) about 3·5 months into the response to bexarotene but before end-of-treatment visit. Total duration of response, including after receipt of methotrexate, was 4·4 months. ‡Percentage in each subcategory in the total column is based on the number of patients in each disease subtype. §One patient in each group had incomplete staging data and are not included in the table: one patient in the brentuximab vedotin group had partial response and one patient in the physician's choice group had no response.

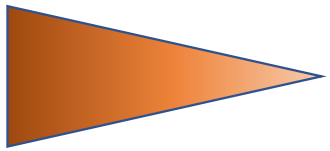
Table 2: **Patient responses by clinical stage at baseline**





Low Dose TSEBI (103 pts) - Morris, IJROBP 2017

CONVENTIONAL DOSE TSEBI



LOW-DOSE TSEBI

From a “save it until you need it” approach…

… to an upfront and repeated use!!

MICOSI FUNGOIDE

Unilesionale

- Radioterapia prima linea
- 20- 24 Gy (frazionamento convenzionale)
- A scopo “curativo” margini ≥ 2 cm

(Micaily 1998, Wilson 1998, Specht 2015)

Palliativa

-8Gy singola frazione

-12Gy 6Gy/die

-9-15Gy 3Gy/die

-10-16Gy 2Gy/die

- **Stadio Ib-IIa**

- Se refrattario a fotochemioterapia (PUVA) +/- IFN +/- retinoide orale o rexinoide (Bexarotene)
- Se controindicazione a fotochemioterapia (PUVA) +/- IFN +/- retinoide orale o rexinoide (Bexarotene)
- RT localizzata (palliazione? lesioni refrattarie) 15Gy in 5# o 12Gy in 2#
- TSEBI utile in caso di sintomi cutanei o malattia generalizzata (eventuale boost pre-TSEBI se placche di elevato spessore)

Stadio IIB Nodulo- tumorale

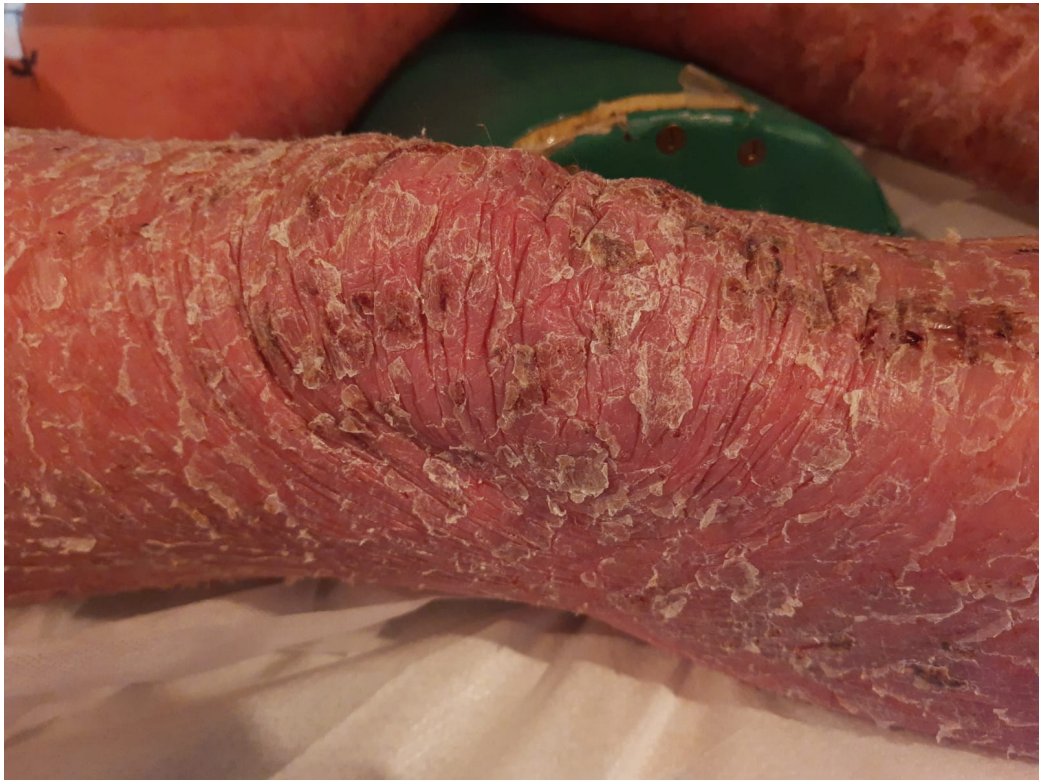
- RT localizzata (Se monoterapia 20-24 Gy o analogo ipofrazionato)
- TSEBI preceduta da boost di debulking su lesione che eccedono lo spessore utile (dosi da 8Gy s.f. a 20Gy)

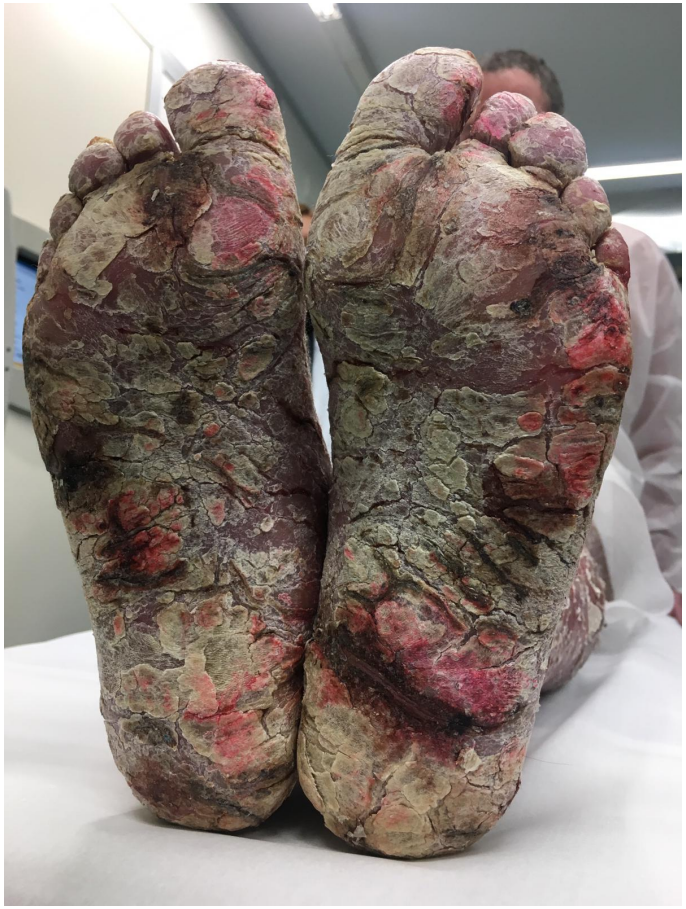
Stadio III (eritrodermico)

- Valutare TSEBI in casi refrattari a fotoaferesi o chemoterapia (monoterapia o combinazione) (almeno 20 Gy)

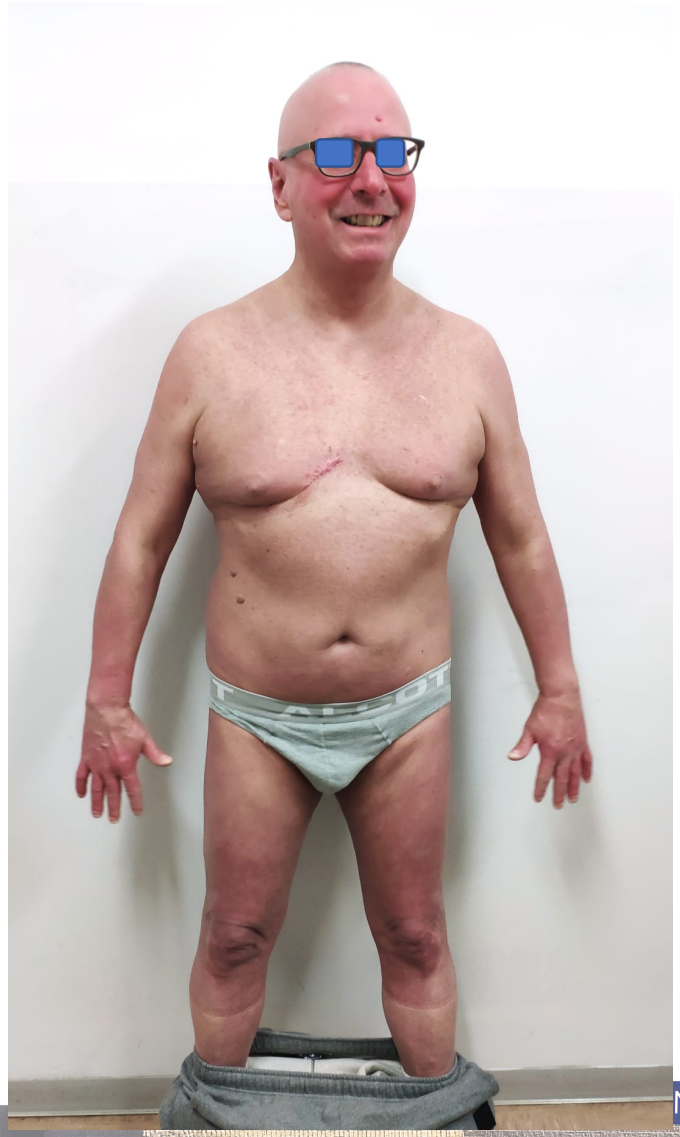
Stadio IV

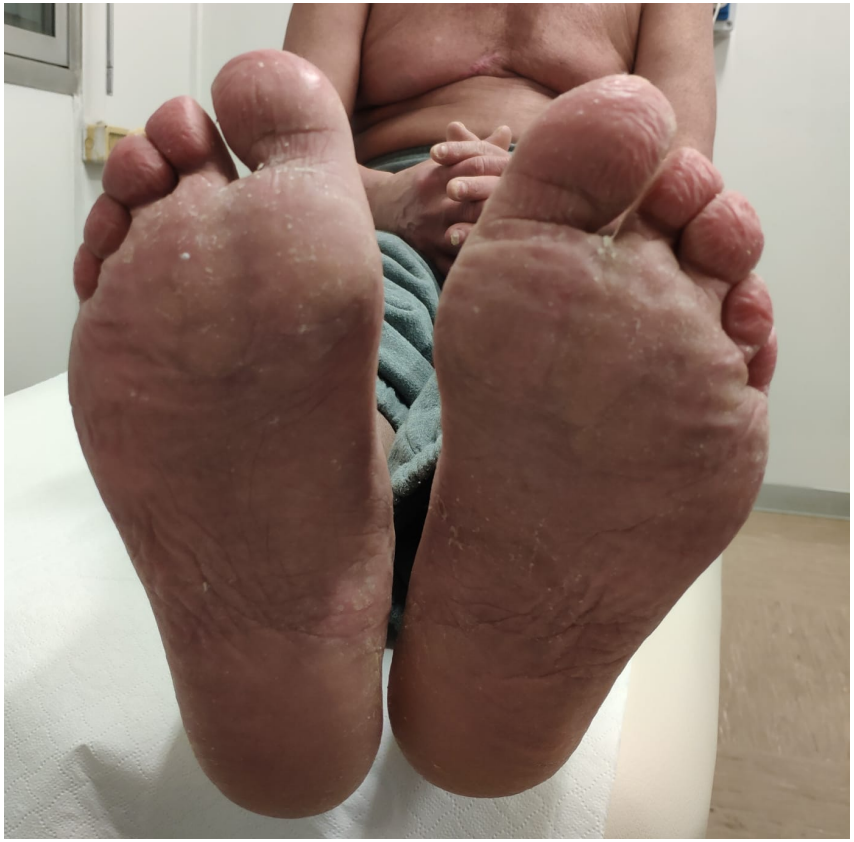
- Ruolo della RT per la palliazione
- RT localizzata o TSEBI a seconda dello stadio T come visto in precedenza





- 59 anni, MF
- Bexarotene+fotoaferesi senza risposta
- Trattato con TSEBI, 20Gy






GLI HO PROPOSTO UNA TERZA LINEA CON ...
DOVEVI PROPORGLI LA TOTAL SKIN IRRADIATION!!!

LINFOMA PRIMITIVO CUTANEO ANAPLASTICO GRANDI CELLULE

Review article

EORTC, ISCL, and USCLC consensus recommendations for the treatment of primary cutaneous CD30-positive lymphoproliferative disorders: lymphomatoid papulosis and primary cutaneous anaplastic large-cell lymphoma*

Werner Kempf,[1,2] †Katrin Pfaltz,[2] †Maarten H. Vermeer,[3] Antonio Cozzio,[1] Pablo L. Ortiz-Romero,[4] Martine Bagot,[5] Elise Olsen,[6] Youn H. Kim,[7] Reinhard Dummer,[1] Nicola Pimpinelli,[8] Sean Whittaker,[9] Emmilia Hodak,[10] Lorenzo Cerroni,[11] Emilio Berti,[12] Steve Horwitz,[13] H. Miles Prince,[14] Joan Guitart,[15] Teresa Estrach,[16] José A. Sanches,[17] Madeleine Duvic,[18] Annamari Ranki,[19] Brigitte Dreno,[20] Sonja Ostheeren-Michaelis,[2] Robert Knobler,[21] Gary Wood,[22] and Rein Willemze[3]

Table 3. PCALCL: therapies and results

Therapy	References	No. of patients	CR, no. (%)	Relapse rate, no. (%)
SE	8,21-25,27-29,36	53	27/27 (100)	19/44 (43)
RT	8,21-23,25,30-35	32	19/20 (95)	9/22 (41)
Multiagent chemotherapy	21,24,25,27,28,37,39-43,45,57,102,103	53	35/39 (90)	16/26 (62)

Kempf, Blood 2011

LINFOMA PRIMITIVO CUTANEO ANAPLASTICO GRANDI CELLULE

Lesione unica o multiple locoregionali (T1 e T2)

- 24-30 Gy o ipofrazionamento equivalente ***(Specht 2015)***

Lesioni multiple disseminate (T3)

- Valutare RT locale per palliazione o TSEBI

➢ *SUBCUTANEOUS PANNICULITIS-LIKE T-CELL LYMPHOMA*

-Trattamento con radioterapia efficace, pochi casi riportati generalmente con dosi >=40Gy.

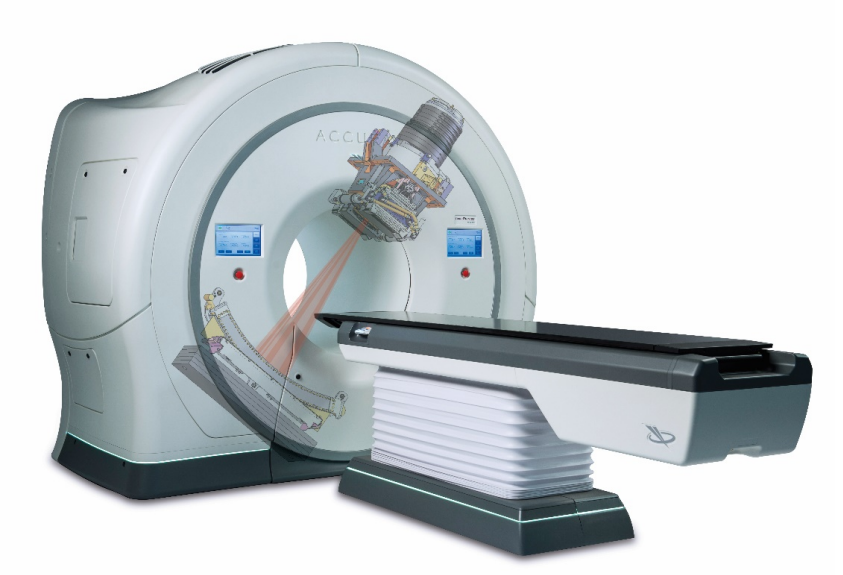
➢ *PRIMARY CUTANEOUS γ/δ T-CELL LYMPHOMA*

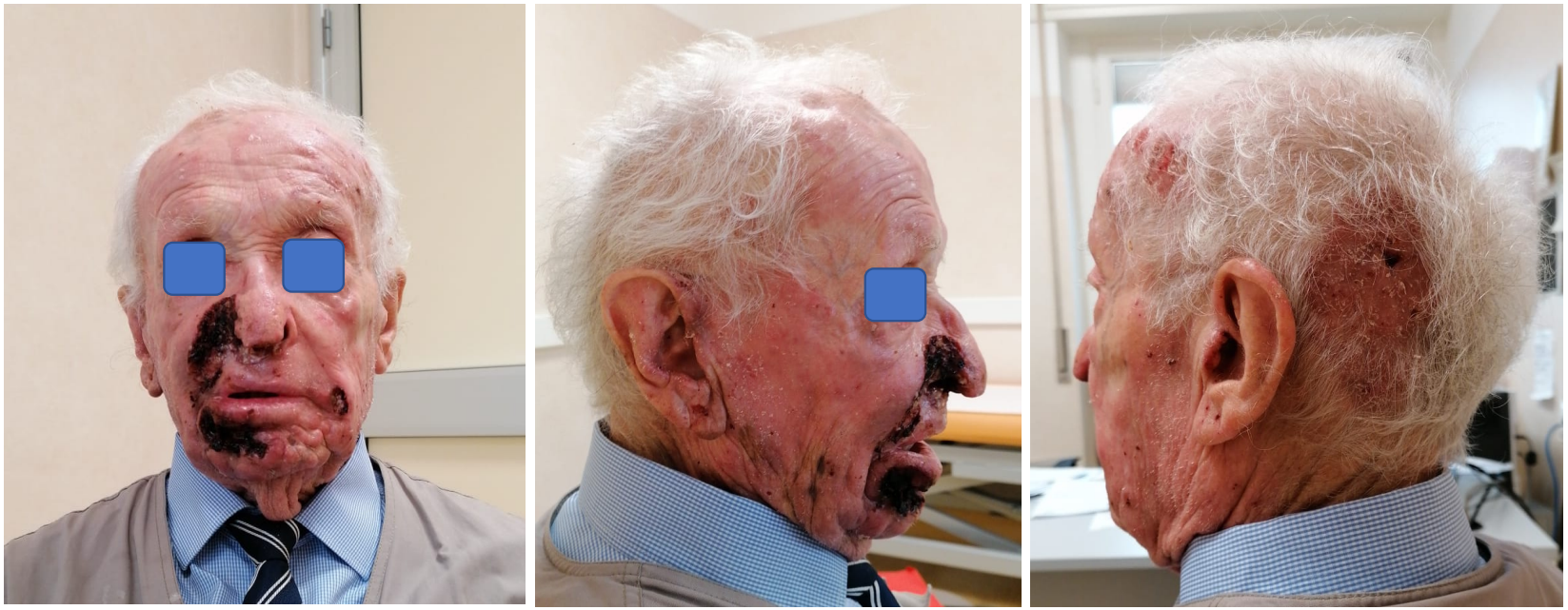
-Spesso presentazione con lesioni multiple, ottimo controllo locale con RT con dosi di 24-30Gy, ma tendenza a recidiva

➢ *PRIMARY CUTANEOUS NK/T-CELL NASAL TYPE*

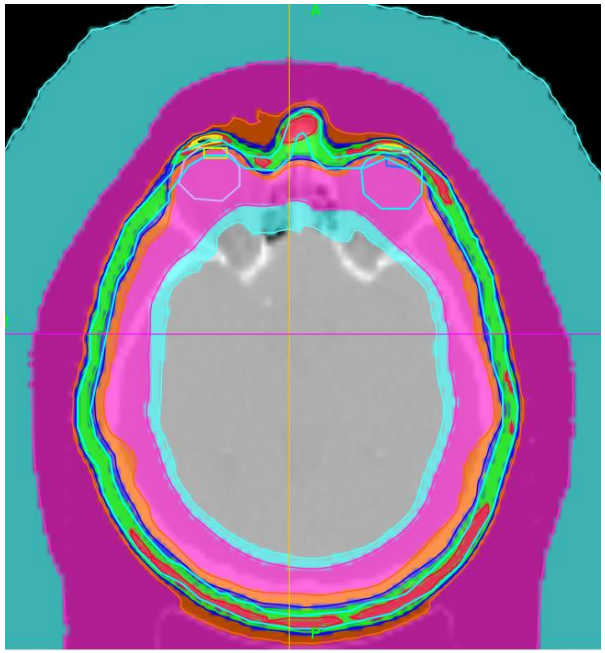
-Istologia radioresistente, Dosi raccomandate di 50-60Gy-

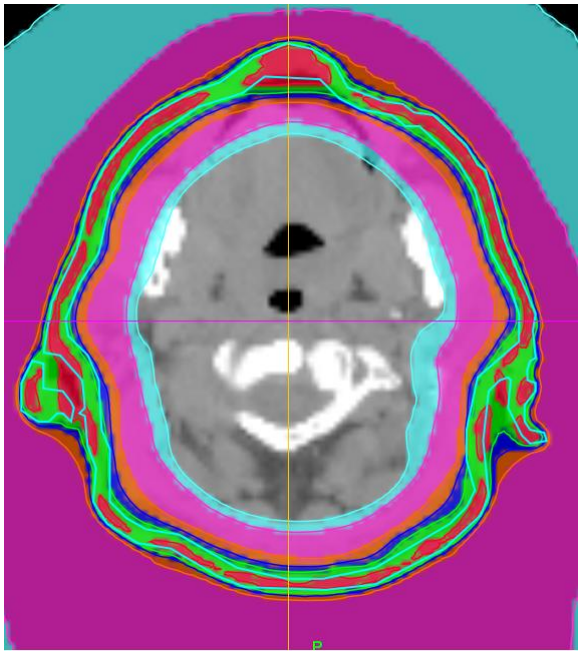
…. E LE NUOVE TECNOLOGIE?!?

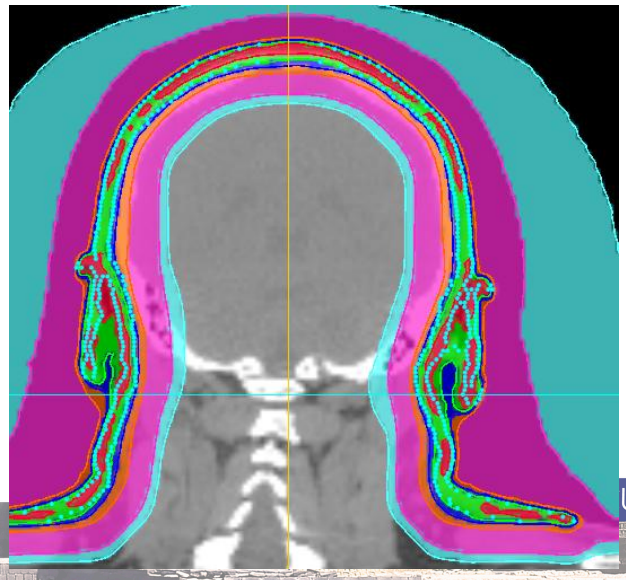


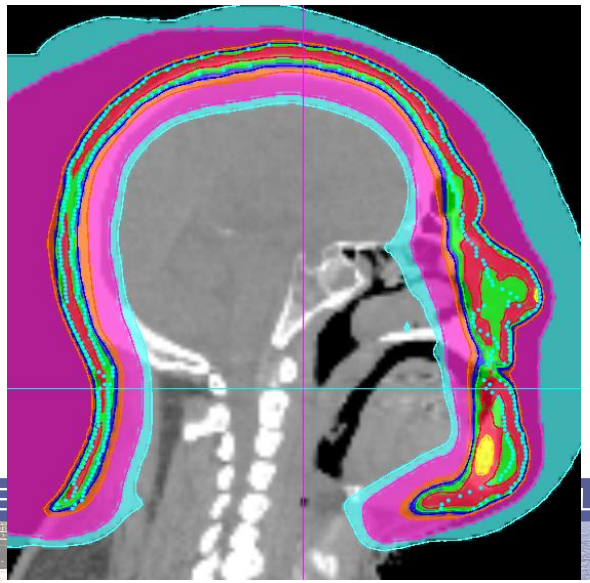


- Uomo, 91 anni, MF modesti aspetti follicolotropismo, comorbidità cardiologica rilevante
- Precedenti trattamenti con RT locale
- Terapia con Gemcitabina interrotta dopo due cicli per scarsa tolleranza
- Trattamento di «Total scalp+face irradiation», 20Gy in 10 sedute con Tomotherapy









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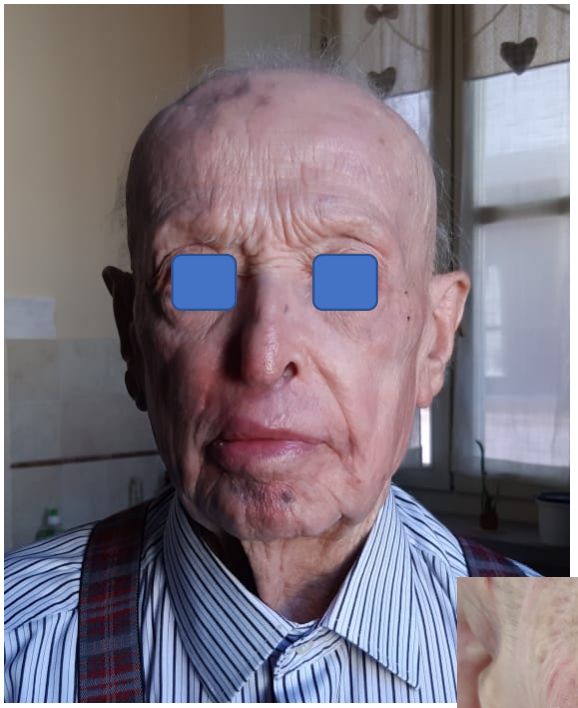
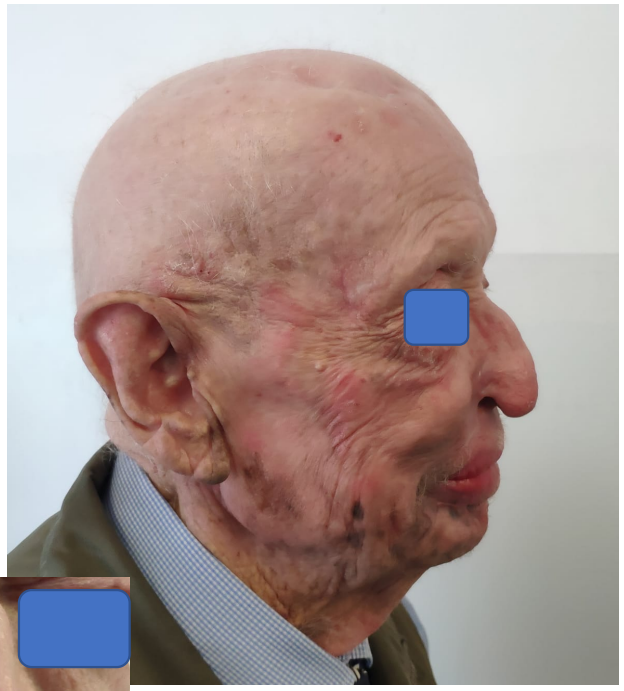
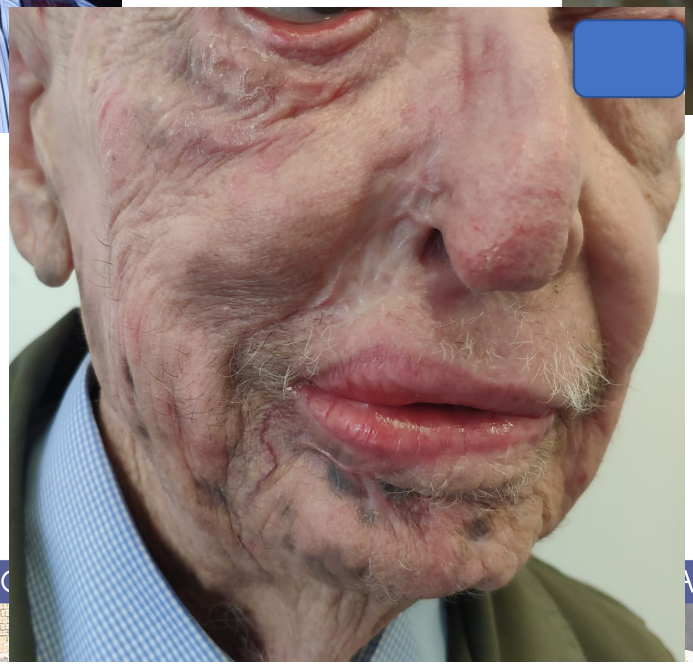
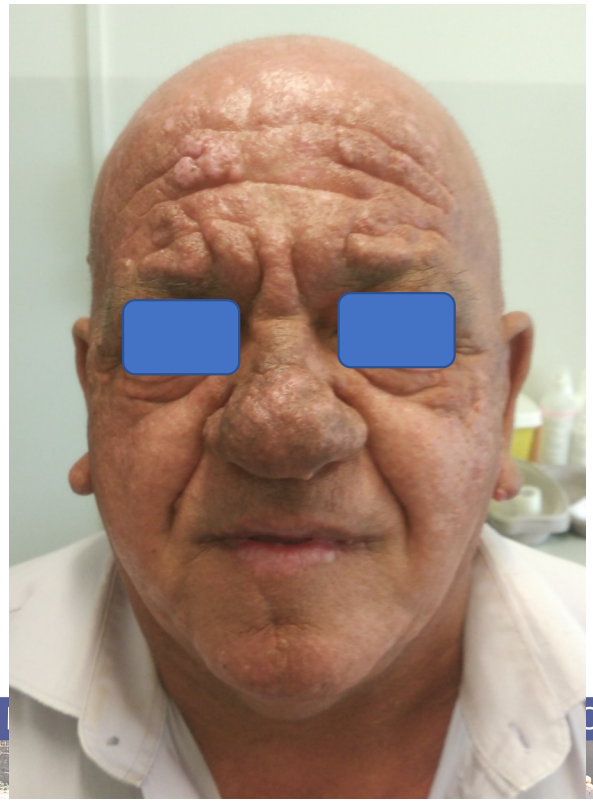
LINARITÀ OTTIMIZZA IL RISULTATO

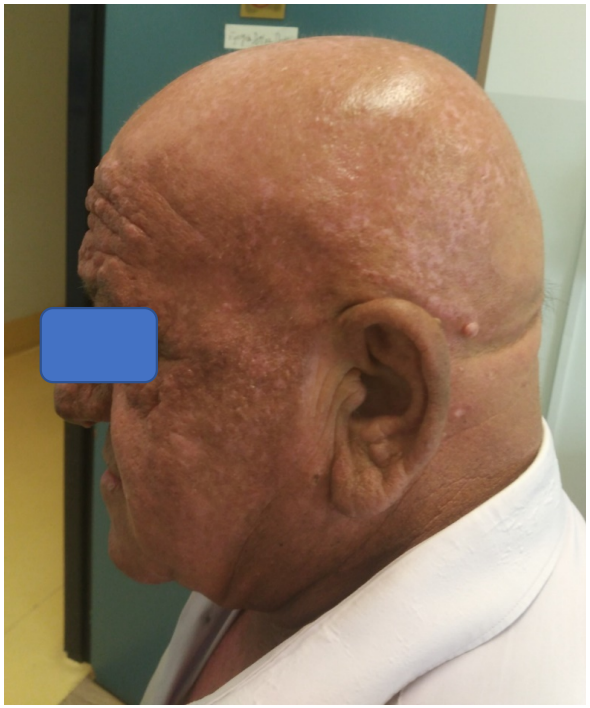


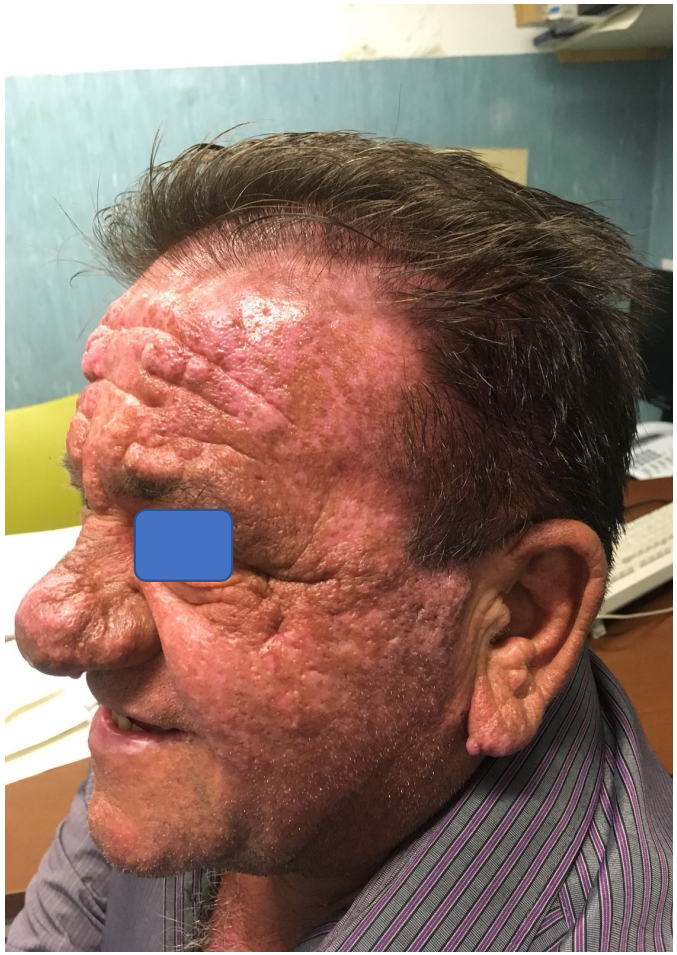


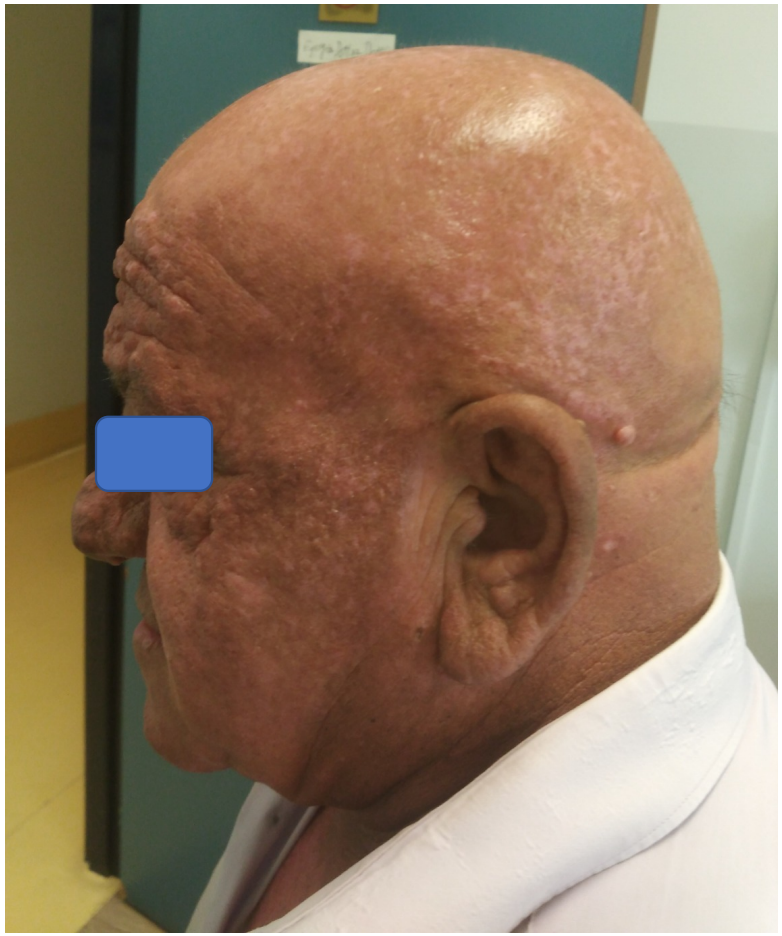


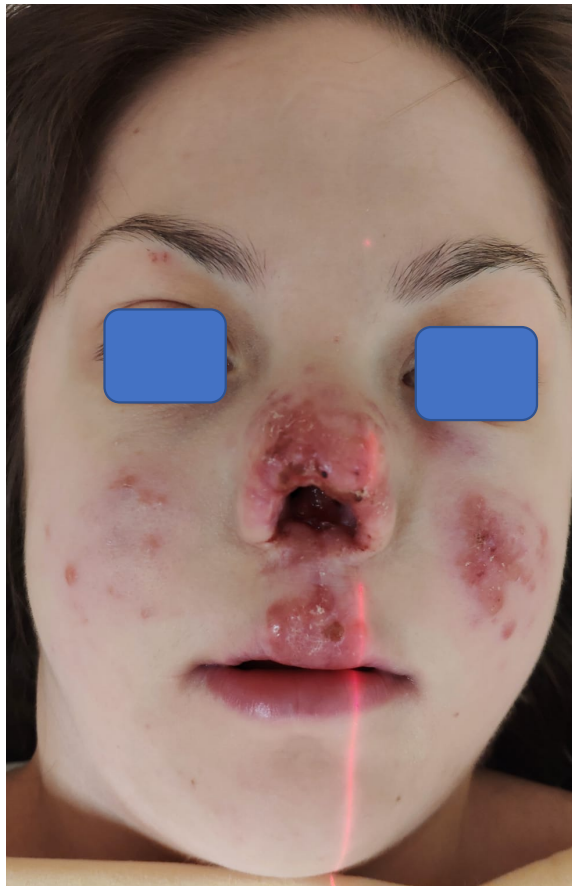
- Uomo, 58 anni
- MF follicolotropa
- «Total scalp+face irradiation» 14Gy in 7 frazioni su volto, scalpo e collo con Tomotherapy

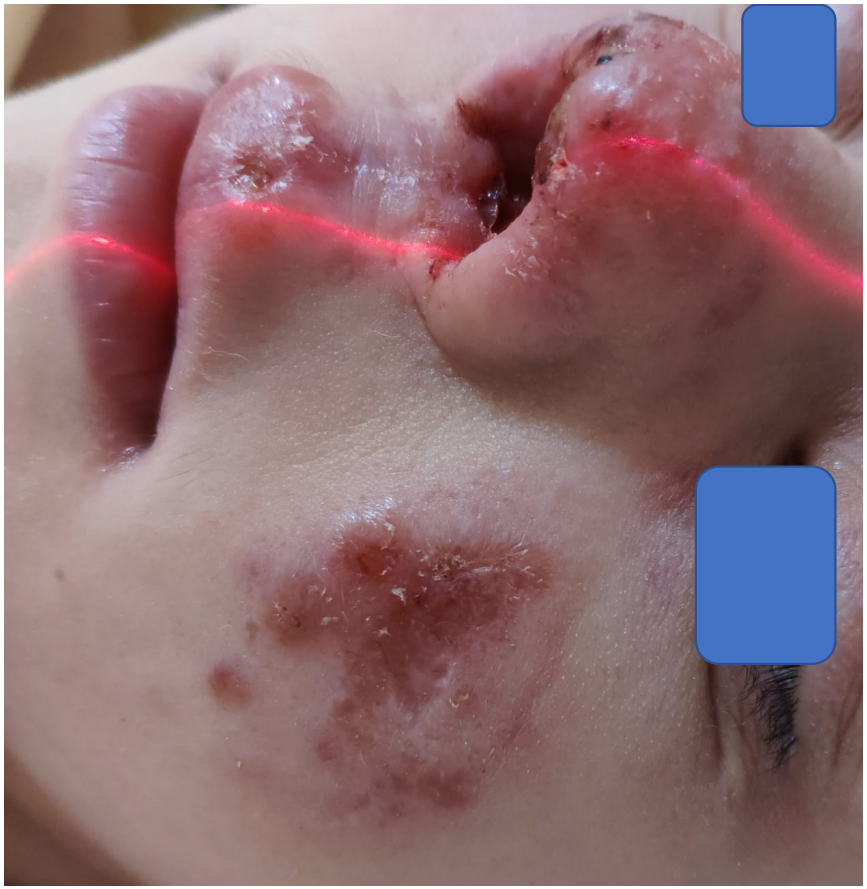




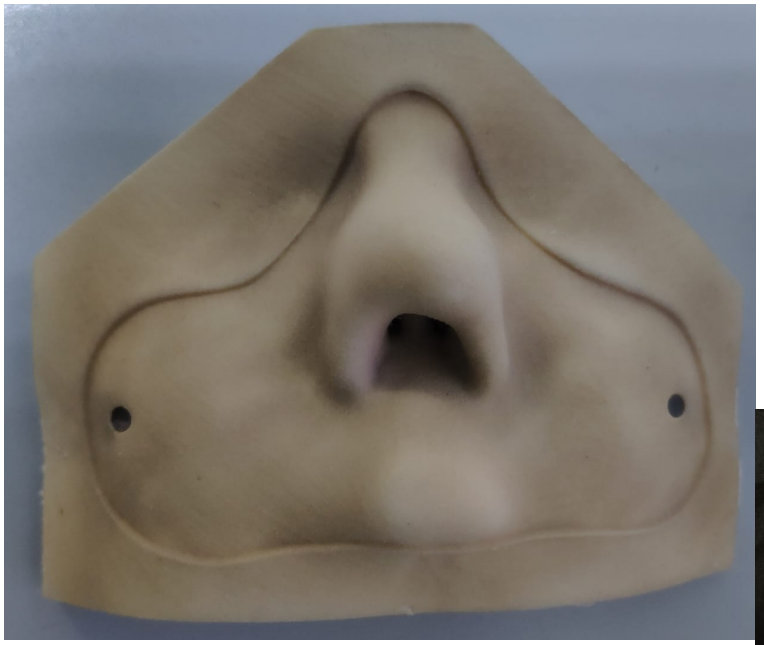


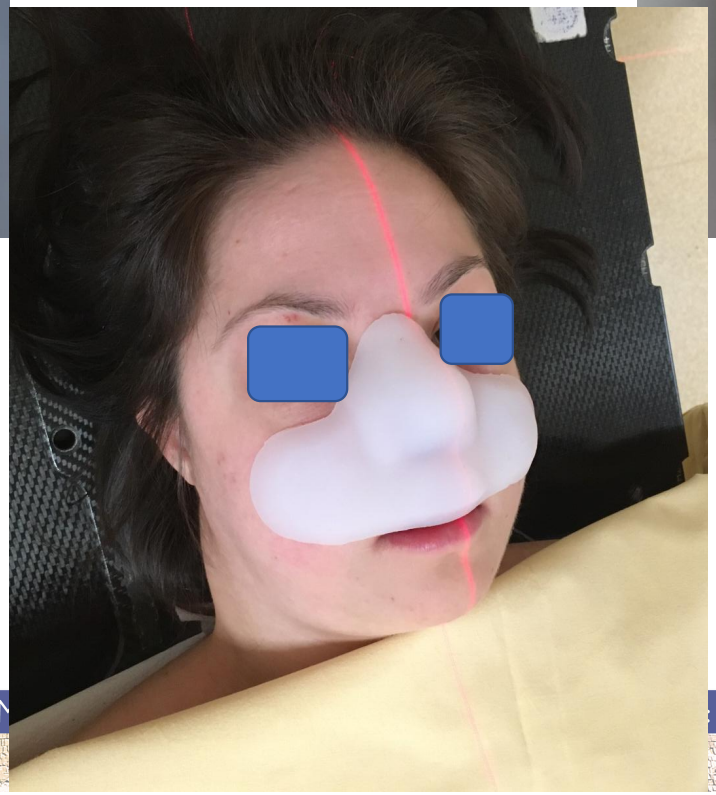


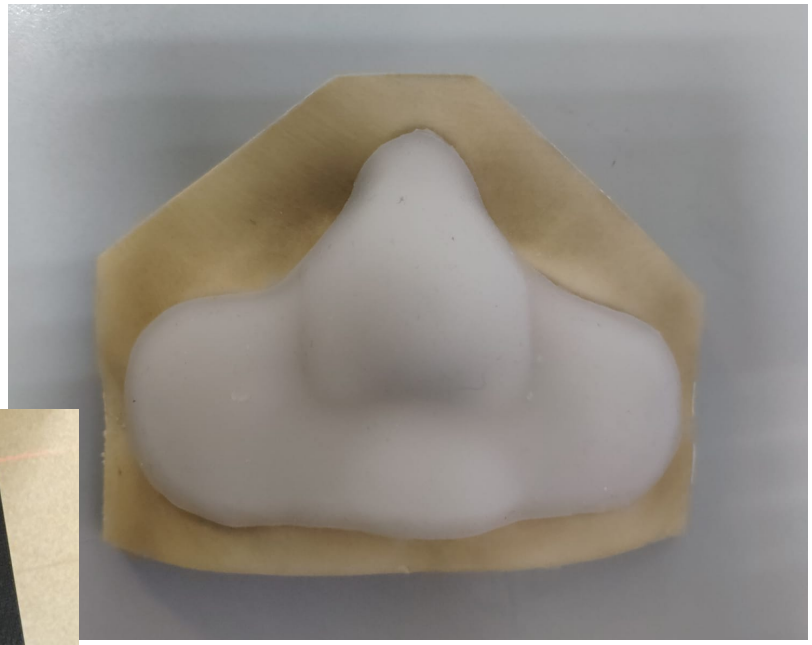


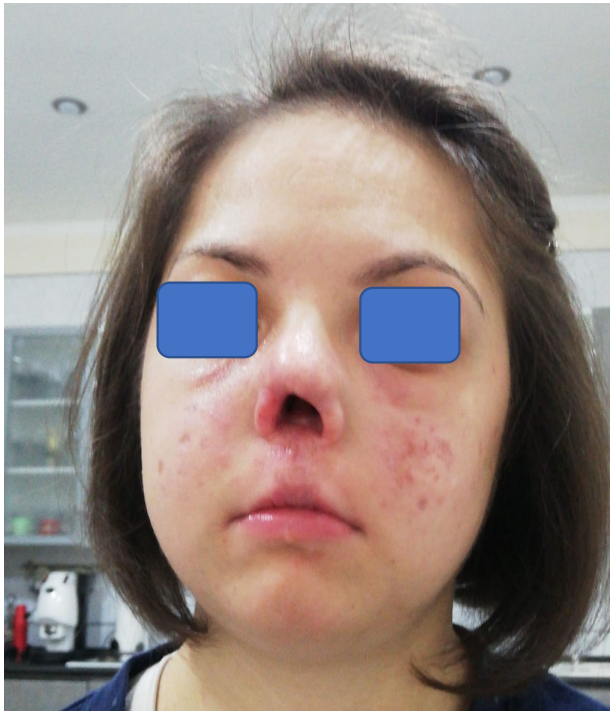


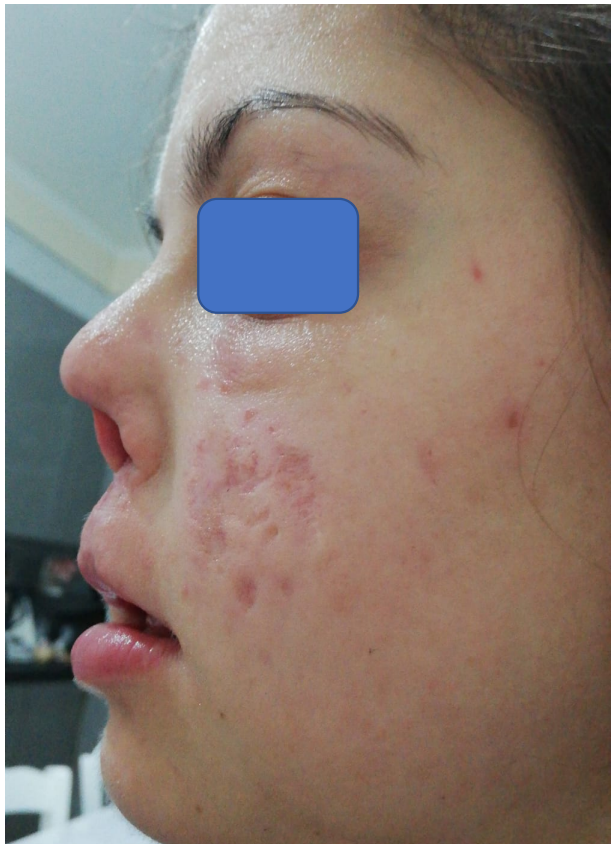
- 26 anni, S. di Down, linfoma a cell T CD8+ tipo Peripheral T cell Lymphoma
- RM: aree di ispessimento tissutale dei tess molli del volto e cartilagini nasali in prevalenza a sx dove si approfonda maggiormente.

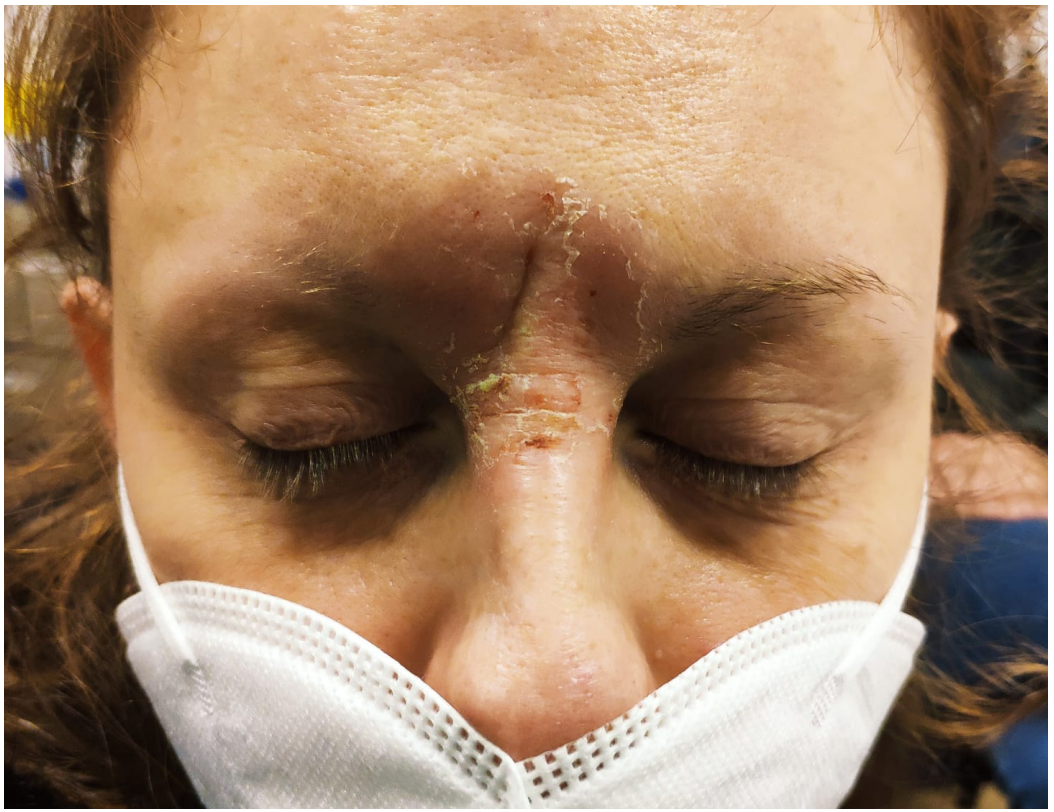




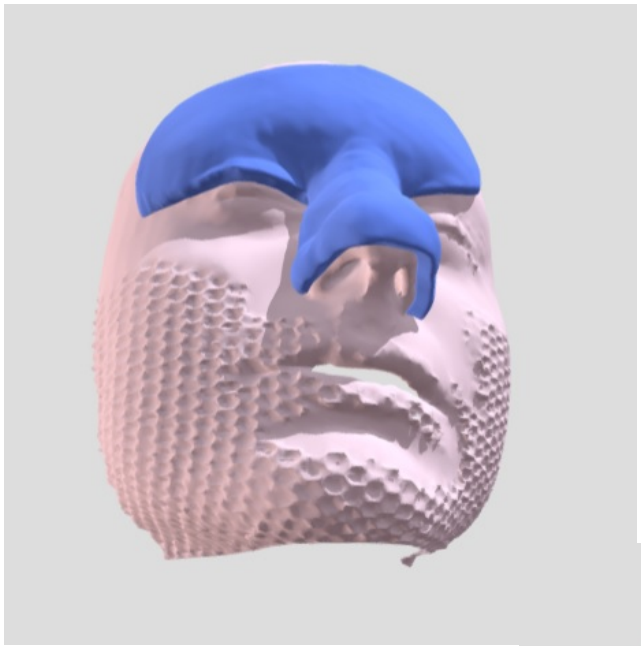


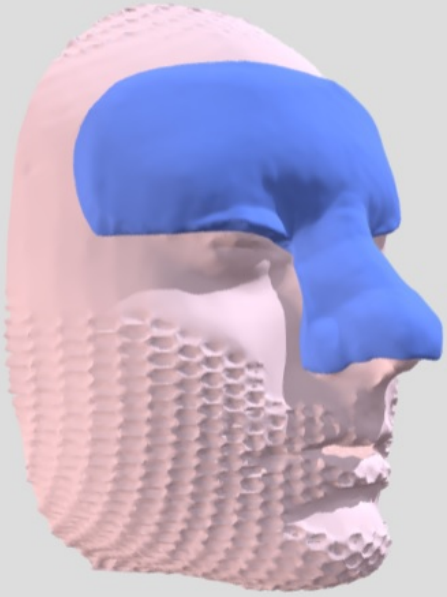


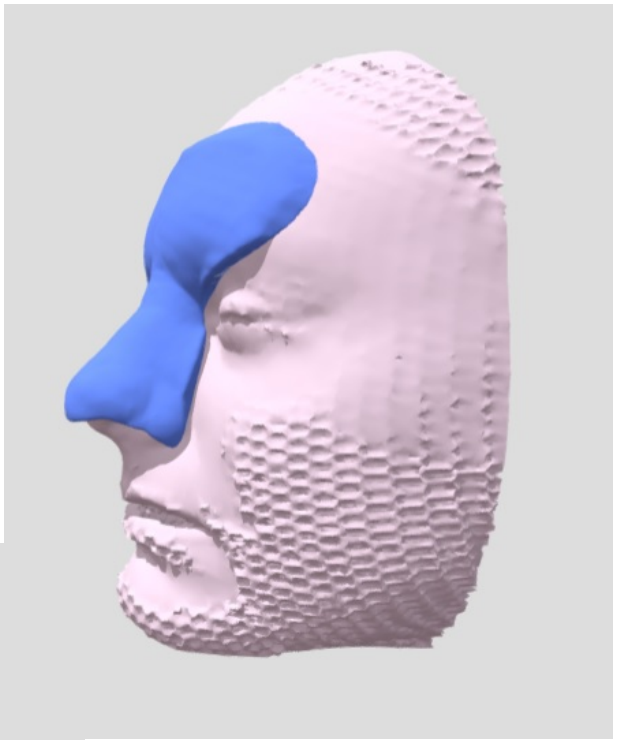


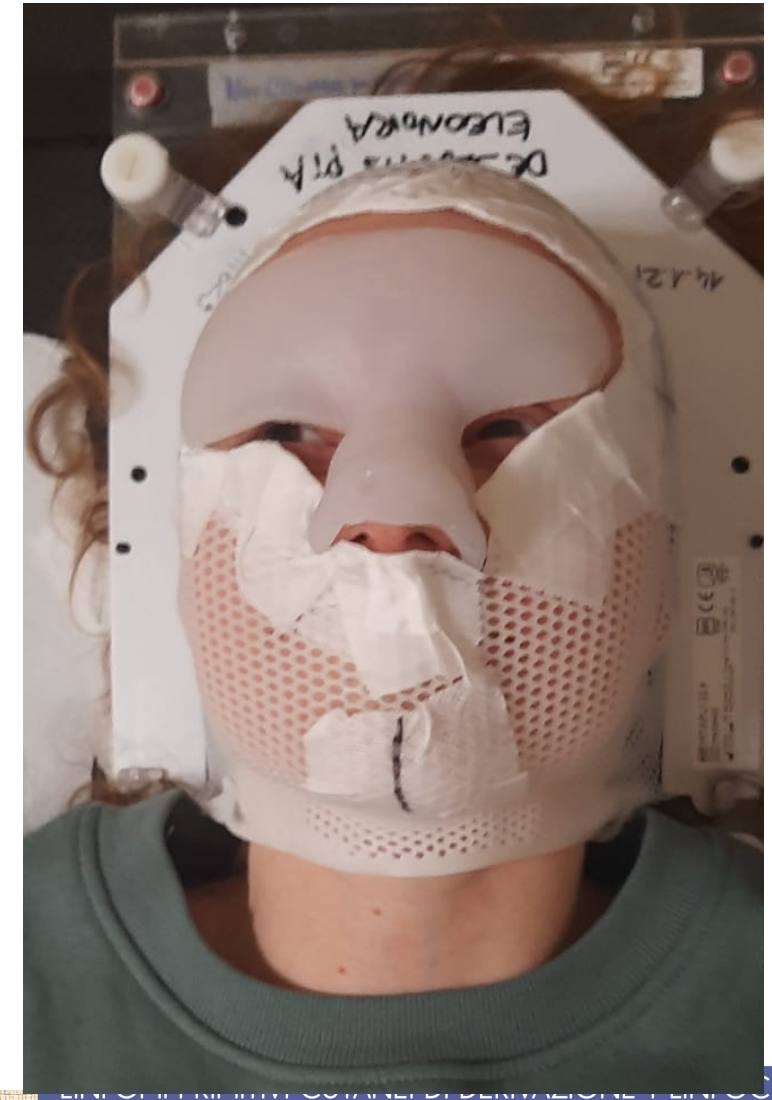


- Ragazza di 14anni, MF unilesionale a livello della regione glabella-piramide nasale, epilazione completa del sopracciglio dx
- RT 24Gy con Tomotherapy e bolus personalizzato







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