RADIOTHERAPIE EN REGARDS CROISES CONTACT/HAUTE ENERGIE

Mardi 8 ctobre 2024

Hôtel Hilton Garden Inn

Nora OUHABRACHE-BOUZID – radiothérapeute (CHU, Bordeaux)

Vincent ATALLAH – radiothérapeute (Centre Clinical, Soyaux)

27e journée des rencontres régionales d'Onco-Dermatologie en Nouvelle-Aquitaine

Liens d'intérêts

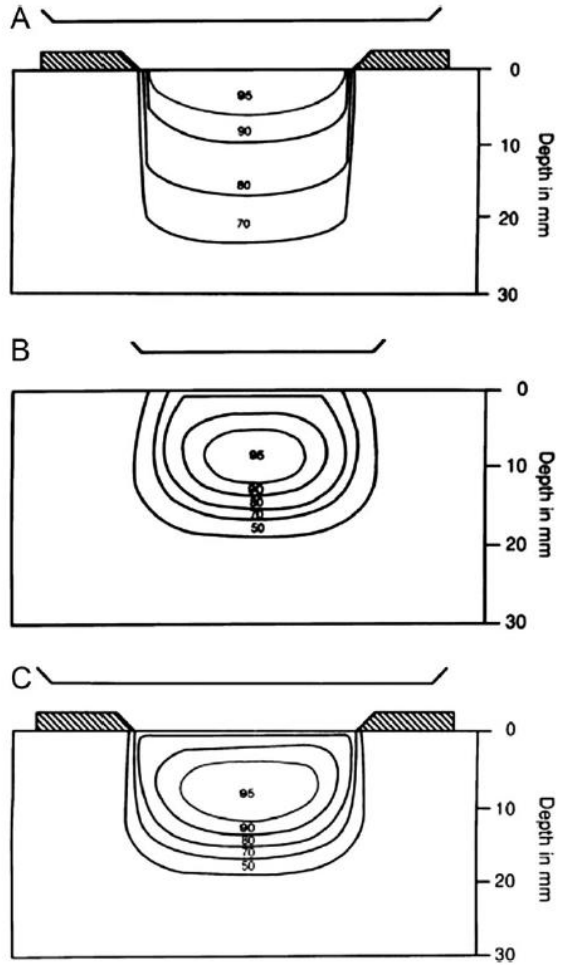
- Nora OUHABRACHE-BOUZID – radiothérapeute (CHU, Bordeaux)
  - Aucun
- Vincent ATALLAH – radiothérapeute (Centre Clinical, Soyaux)
  - MSD,BMS,Regeneron

Techniques de radiothérapie

A chaque technique ses particularités et sa situation clinique

TABLE VII.
Local Control Rates According to External-Beam Technique (339 Patients).[25]

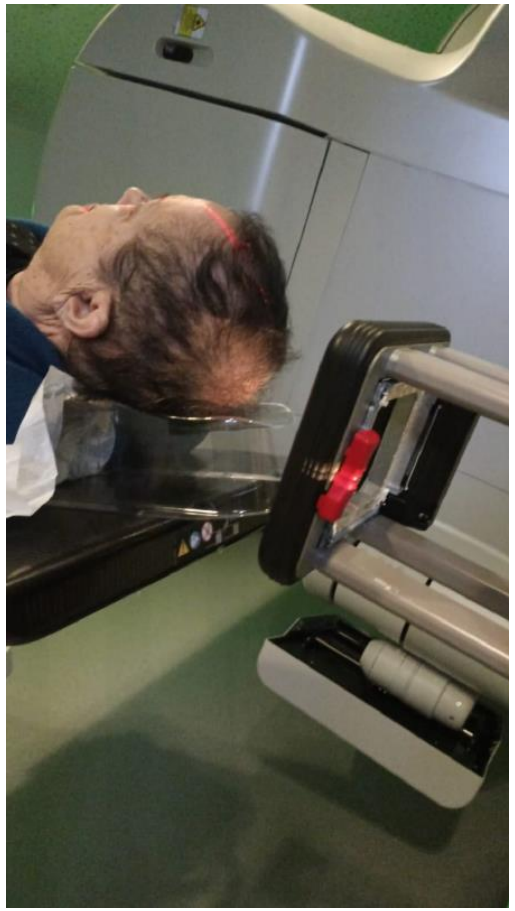
Modality	Size ≤1 cm (%)	Size 1.1–5 cm (%)	Size >5 cm (%)	Size Not specified (%)
Basal cell carcinoma				
Superficial x-ray	69/71 (97)	84/90 (93)	4/4 (100)	3/3 (100)
Electron beam	11/12 (92)	16/22 (73)	4/5 (80)	1/1 (100)
Combination	5/5 (100)	13/16 (81)	5/6 (83)	0/0
Photons (1.2–4 MV)	1/1 (100)	3/5 (60)	0/0	1/1 (100)
Squamous cell carcinoma				
Superficial x-ray	12/12 (100)	10/11 (91)	1/1 (100)	0/0
Electron beam	3/4 (75)	7/10 (70)	3/4 (75)	0/1 (0)
Combination	4/5 (80)	19/26 (73)	4/8 (50)	2/4 (50)
Photons (1.2–4 MV)	2/2 (100)	3/4 (75)	1/3 (33)	2/2 (100)

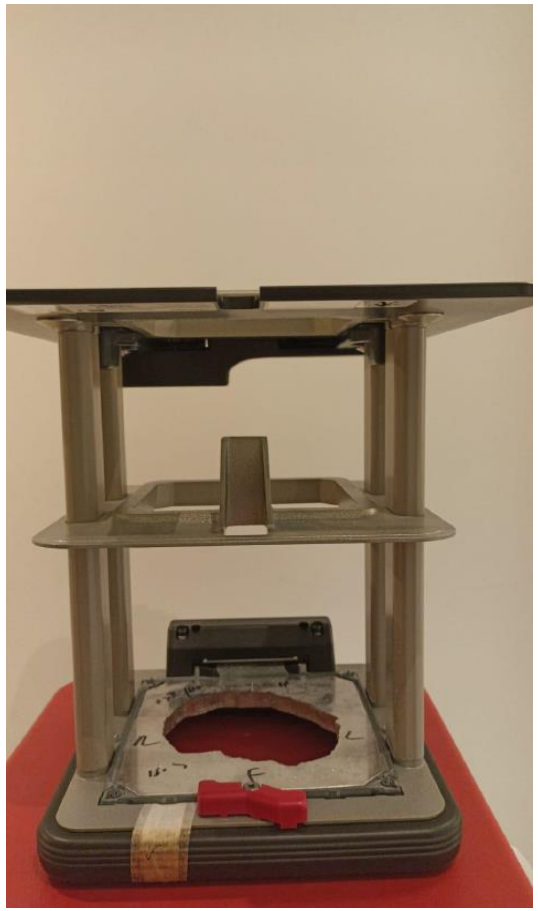


Mendenhall et al. Laryngoscope 2009

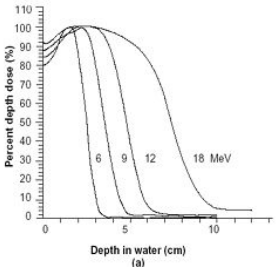
Techniques de radiothérapie

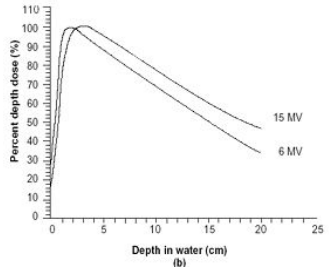
Radiothérapie externe électrons

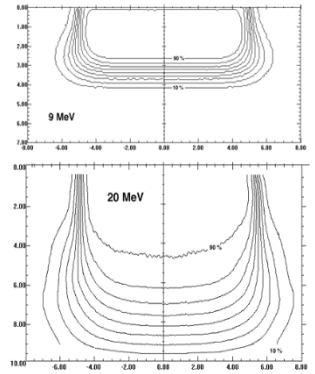




- **Délivré par un accélérateur linéaire**
- **Energies de 6 à 20 Mev**
- **Peut traiter des lésions jusqu'à 5 cm (isodode 90 % pour les faisceaux de 20 MeV)**
- **Clinique ou modélisé par un TPS**
- **Collimateur en plomb standard ou personnalisé**
- **Lesions adaptées:**
  - **lésions larges et profondes d'au moins 1 cm**
- **Défauts:**
  - **Épargne dosimétrique dans les premiers millimètres**
  - **Dose latérale (surtout à 20 Mev)**



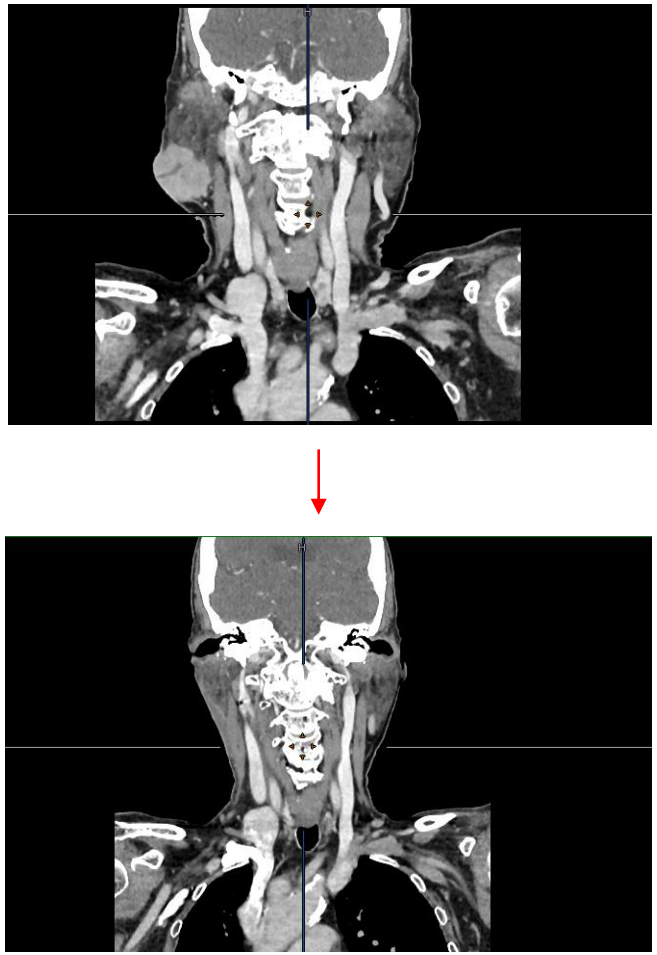


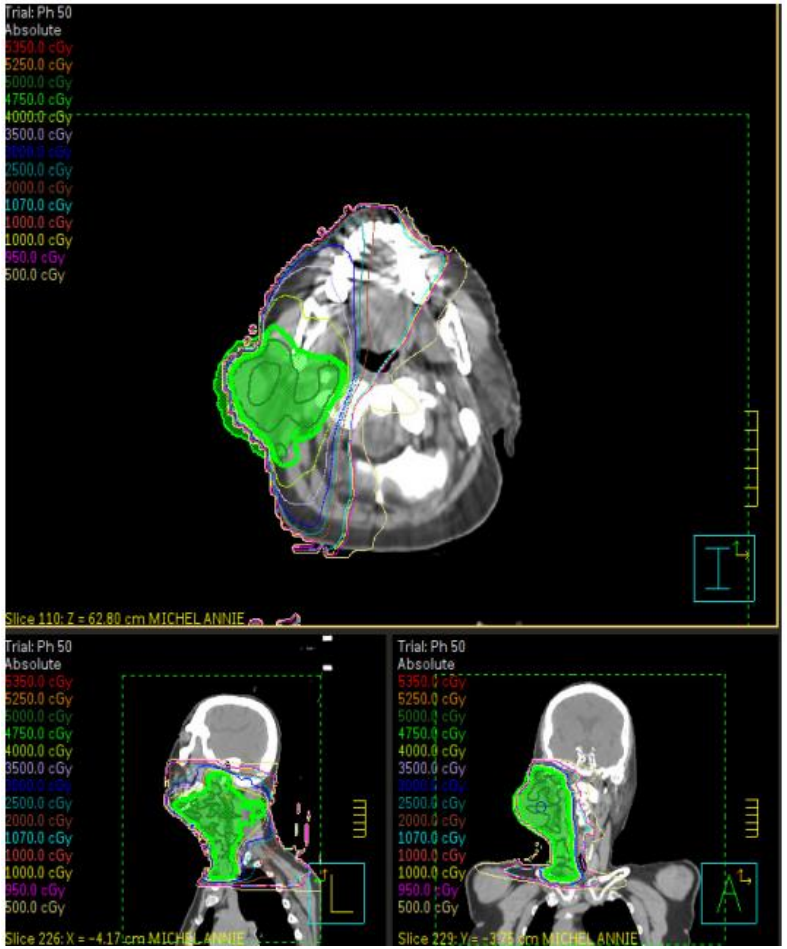


Yosefof et al. Cancers 2023

Techniques de radiothérapie

Radiothérapie externe Photons





- **Mega-Voltage (MV) photon beam therapy:**
- **Délivré par des accélérateurs linéaires de 6-18 MeV**
- **Plannifié par TPSA**
- **Permet un traitement complexe conformationnel et une meilleure précison dosimétrique**
- **Lesions adaptées:**
  - **lésions profondes à proximité organes critiques**
- **Défauts:**
  - **Épargne dosimétrique dans les premiers mm (nécessité de bolus techniquement complexe)**

Techniques de radiothérapie

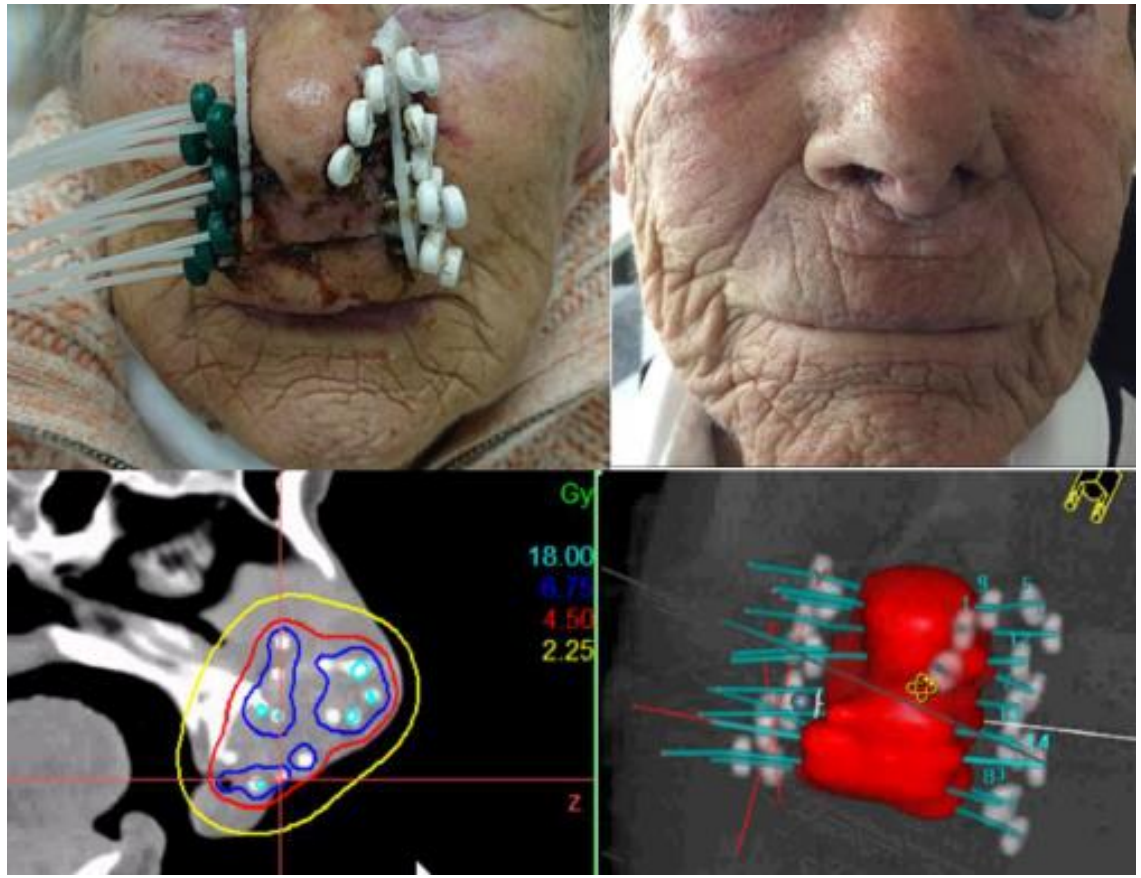
Contacthérapie ou radiothérapie faible énergie (meillure définition)

- **Cône d'application placé au contact de la surface à traiter.**
- **Energie entre 30 et 300 Kv**
- **EN réalité definition très (trop) large car correspond à différentes modalités de machine et d'énergie (Grenz Ray, radiothérapie superficielle, orthovoltage)**
- **Lesions adaptées:**
  - **Lésions superficelles et bien délimitées jusqu'à 1 cm de profondeur**
  - **A proximité des organes superficiels à protéger (exemple : Oeil)**
- **Défauts:**
  - **Difficultés à évaluer et traiter l'extension microscopique et en profondeur (mais ça change ….)**

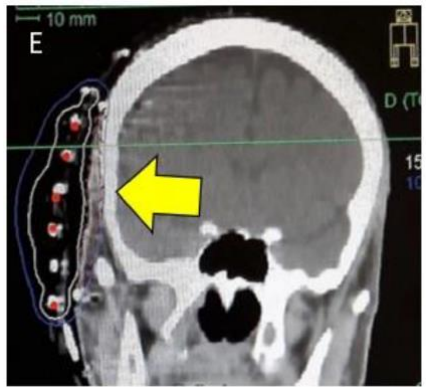
Yosefof et al. Cancers 2023

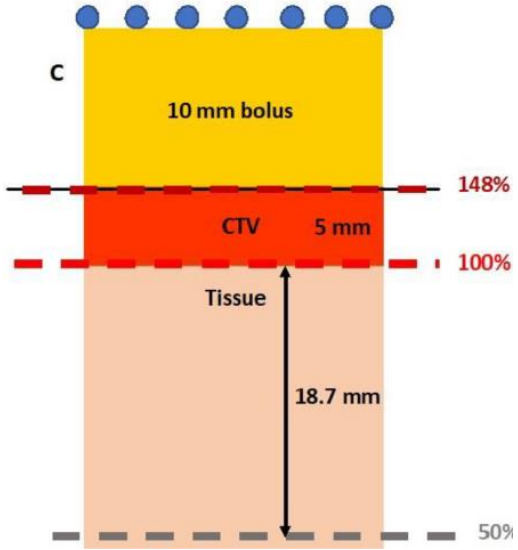
Techniques de radiothérapie

Curiethérapie interventionnelle



- **De plus en plus réalisé avec des catheters et des sources HDR ou avec des moules**
- **Lésions adaptées**
  - **Lésions superficielles complexes à proximité direct d'organes critiques**
  - **Rattrapage**
- **Défauts:**
  - **Plateau technique peu diffusé**
  - **Limitation relative en volume**

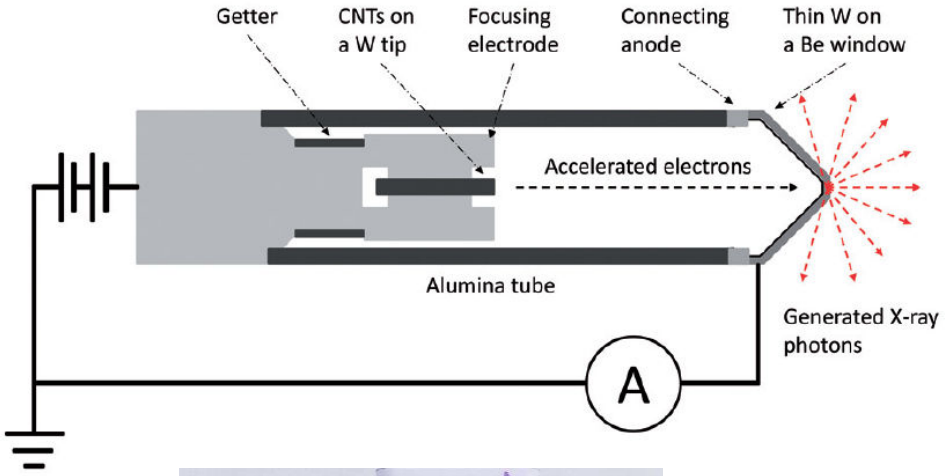




Guinot et al. Radiot Oncol 2018

Techniques de radiothérapie

Curiethérapie électronique



- **Energie entre 10 et 90 Kv (généralement 50)**
- **Applicateurs entre 10 et 50 mm**
- **Faible énergie donc :**
  - **peu de pénétration en profondeur donc dose par séance plus forte (moins de séances)**
  - **Opérateur reste dans la salle**!
- **Défauts:**
  - **Dose moins uniforme que la curiethérapie classique**
  - **Temps physique plus long**

Pashadazeh et al. J dermato Treatment 2019

Gerard et al. Cancer Radiot 2020

Techniques de radiothérapie

Comparaison des techniques

Table 1. Physical parameters of the standard radiation therapy modalities used in skin cancer management.

Parameters	Radionuclide Brachytherapy (data for I-192)	Electronic brachytherapy(data for Xoft® Axxent® System)	Superficial X-ray therapy	Orthovoltage radiation therapy	Electron beam therapy
Radiation	Gamma photons	X-ray photons	X-ray photons	X-ray photons	Electron beam
Energy/Voltage	380 keV	50 kV	50–150 kV	150–300 kV	6–15 MV
Source to skin distance (cm)	0.5–1.5	2-3	10–30	50	100
90% isodose line (cm)	<1	<1	0.5	2	3–5
Shielded room	Yes	No	Yes	Yes	Yes

Table 4. Percent depth dose of radionuclide brachytherapy with Ir-192.

Depth (mm)	0.5	1.5	3	4	5	7	10	15	20
PDD	132.8%	117.9%	100%	90.3%	81.6%	67.9%	52.4%	32.4%	26.6%

Table 5. Percent depth dose of the Esteya electronic brachytherapy system with 10 mm surface applicator.

Depth (mm)	0	1	2	3	4	5	6	7	8	9	10
PDD	100%	92.7%	87.6%	80.1%	73.1%	68.6%	63.8%	59.1%	55.9%	51.7%	48.5%

Table 6. Percent depth dose comparison of orthovoltage X-ray and electron beam.

Depth (mm)	10	20	30	40
PDD – 250 kV X-ray	80%	62%	52%	46%
PDD – 6 MV electron beam	86%	53%	4%	1%

Pashazadeh et al. Journal of Dermatological Treatment 2019

Radiothérapie de contact

Une histoire avant tout de dermatologues

Arch Dermatol. 1975 Nov;111(11):1511-7.

Ionizing radiation therapy in dermatology. Current use in the United States and Canada

H Goldschmidt

PMID: 1200660

Abstract

A comprehensive survey of the Task Force on Ionizing Radiation of the National Program for Dermatology was answered by 2,444 dermatologists in the United States and Canada (53.6% of 4,560 questionnaires). Computer analysis of the data showed that 55.5% of dermatologic offices are equipped with superficial x-ray machines and/or grenz ray units and that 44.3% of dermatologists use superficial x-ray or grenz rays regularly. Most respondents (65.8%) favor increased practical instruction in radiotherapy in training programs. A majority (63.4%) want examinations in radiation therapy by the American Board of Dermatology continued or increased. Data dealing with training in radiation therapy, reasons for non-utilization, alternate care, radiation safety, and economic considerations are presented in detail. Common indications for superficial x-ray therapy and grenz ray therapy are listed in order of frequency and percentage of use.

Radiothérapie de contact

Résultats historiques

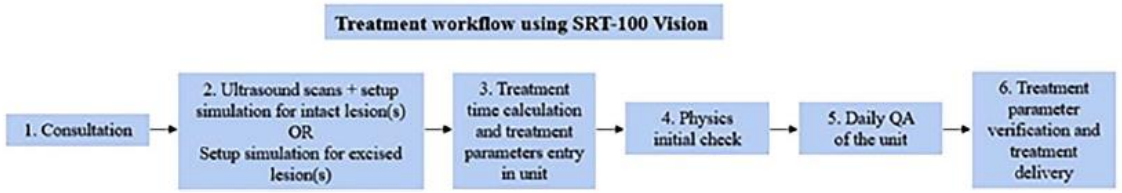
Author	Number of Patients	Pathology	Outcome	Complications	Radiotherapy Modality and Fractionation
Avril 1997 [23]	177	BCC	4 years local control—92.5%	65% dyspigmentation and telangiectasia	Interstitial interventional radiotherapy (brachytherapy)—55% Soft X-ray (contact) radiotherapy—33% Conventional radiotherapy—12%
Locke 2001 [22]	425	T1/T2 BCC + SCC	5 years local control for BCC—94% 4 years local control for SCC—85%	5.8%	Soft X-ray (contact) radiotherapy—60% Electron beam radiotherapy—19% Soft X-ray and electron beam combination—20% Megavoltage—<2%
Schulte 2005 [26]	1267	BCC + SCC	5 years local control for BCC—95.8% 5 years local control for SCC—94%	Hypopigmentation—72.7% Telangiectases—51.5% Ulceration—6.3%	Soft X-ray (contact) radiotherapy—100% 10–100 kV
Barysch 2012 [25]	180	SCC	5 years local control—86.2%		Soft X-ray (contact) radiotherapy—100% 30–60 kV
Cognetta 2012 [24]	1715	BCC + SCC	5 years local control—95%		Soft X-ray (contact) radiotherapy—100% 5 sessions of 7 Gy or 7 sessions of 5 Gy
Bortoluzzi 2022 [27]	56	SCC	5 years local control—71.3%	3%—non-acceptable cosmetic result	Soft X-ray (contact) radiotherapy: 55–60 kV—55% 50–100 kV—39% Other soft X-ray protocol—6%

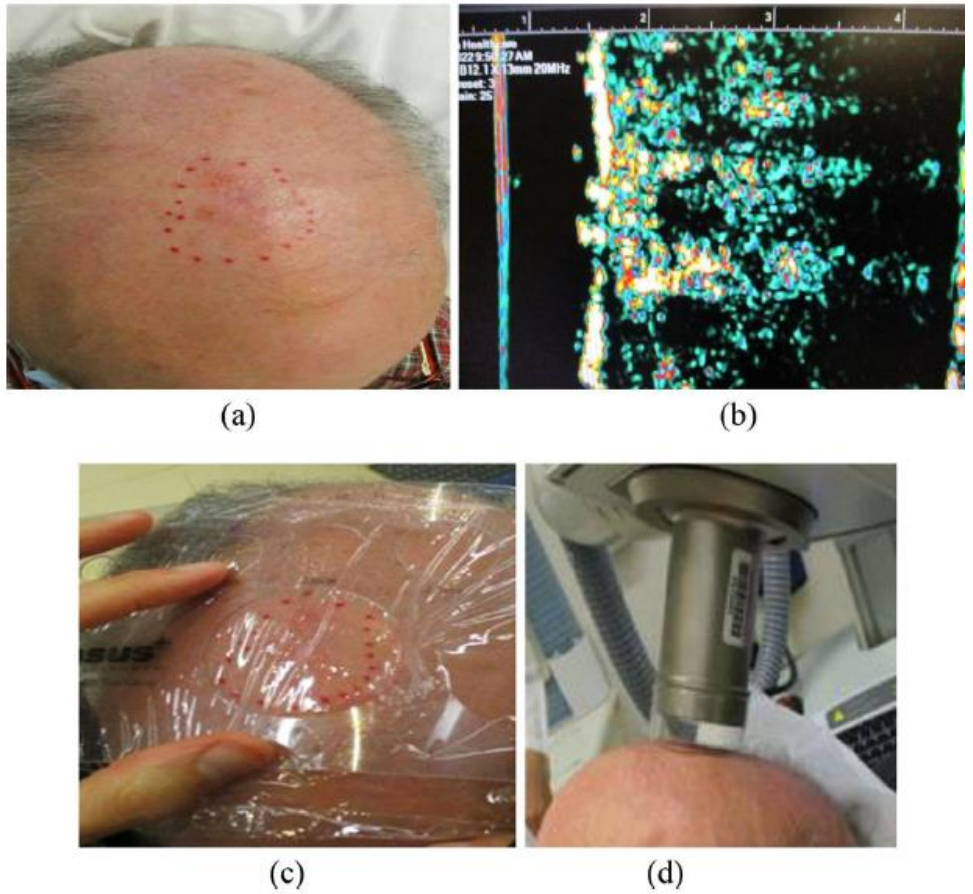
Taux de contrôle historique entre 85 et 95 % pour des lésions peu évoluées localement

Yosefof et al. Cancer 2023

Radiothérapie de contact

Nouvelles modalités : IGSRT





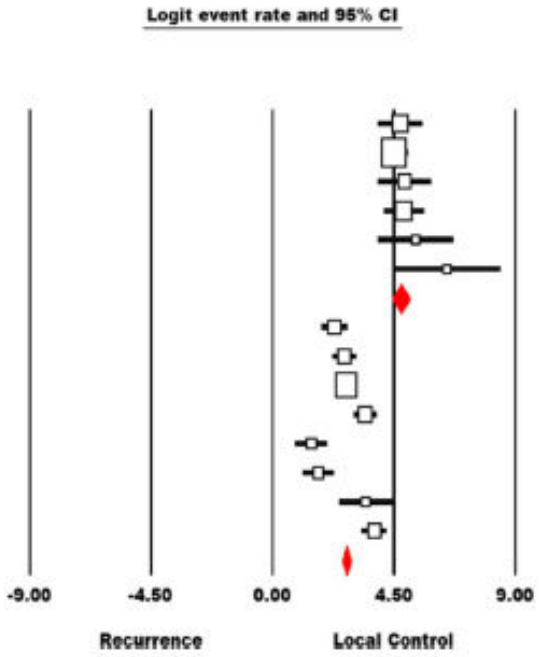
Permet d'évaluer profondeur et infiltration latérale pour choisir précisément énergie et collimateur

Lee et al. J appl Clin Med Phys 2023

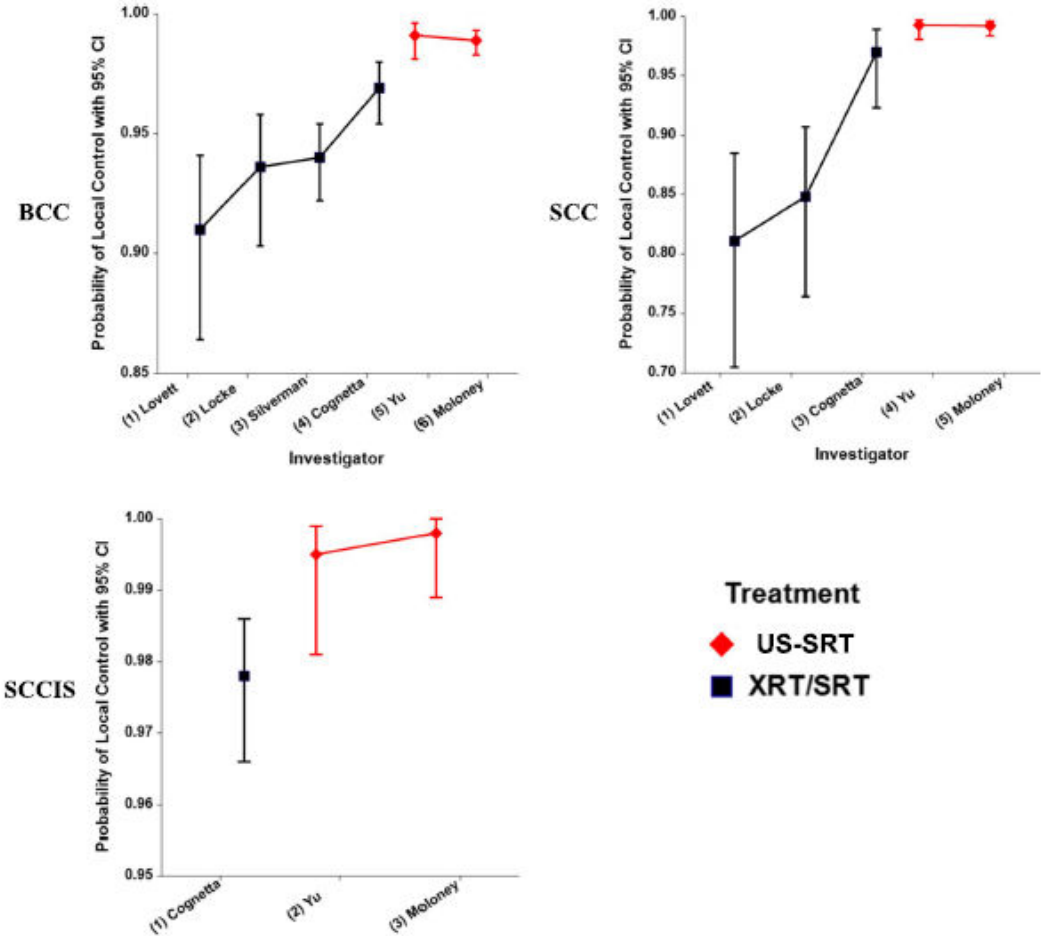
Radiothérapie de contact

Comparaison IGSRT et SRT/EBRT

Study name	Subgroup within study	Total	Logit event rate	Standard error
Yu (BCC)	IGSRT	698 / 704	4.756	0.410
Moloney (BCC)	IGSRT	1471 / 1487	4.521	0.251
Yu (SCC)	IGSRT	544 / 548	4.913	0.502
Moloney (SCC)	IGSRT	926 / 933	4.885	0.379
Yu (SCCIS)	IGSRT	415 / 417	5.335	0.709
Moloney (SCCIS)	IGSRT	649 / 650	6.475	1.001
			4.775	0.167
Lovett (BCC)	XRT/SRT	202 / 222	2.313	0.234
Locke (BCC)	XRT/SRT	305 / 326	2.676	0.226
Silverman (BCC)	XRT/SRT	810 / 862	2.746	0.143
Cognetta (BCC)	XRT/SRT	690 / 712	3.446	0.217
Lovett (SCC)	XRT/SRT	60 / 74	1.455	0.297
Locke (SCC)	XRT/SRT	84 / 99	1.723	0.280
Cognetta (SCC)	XRT/SRT	129 / 133	3.474	0.508
Cognetta (SCCIS)	XRT/SRT	842 / 861	3.791	0.232
			2.747	0.080



All Lesions Contrasts:
Yu US-SRT v. XRT/SRT Studies Combined, Q [1] = 51.5, p < 0.0001
Moloney US-SRT vs. XRT/SRT Studies Combined, Q [1] = 79.3, p < 0.001



Amélioration significative du contrôle local pour différentes histologies : Nouveau standard thérapeutique

Yu et al. Discover Oncology (2022)

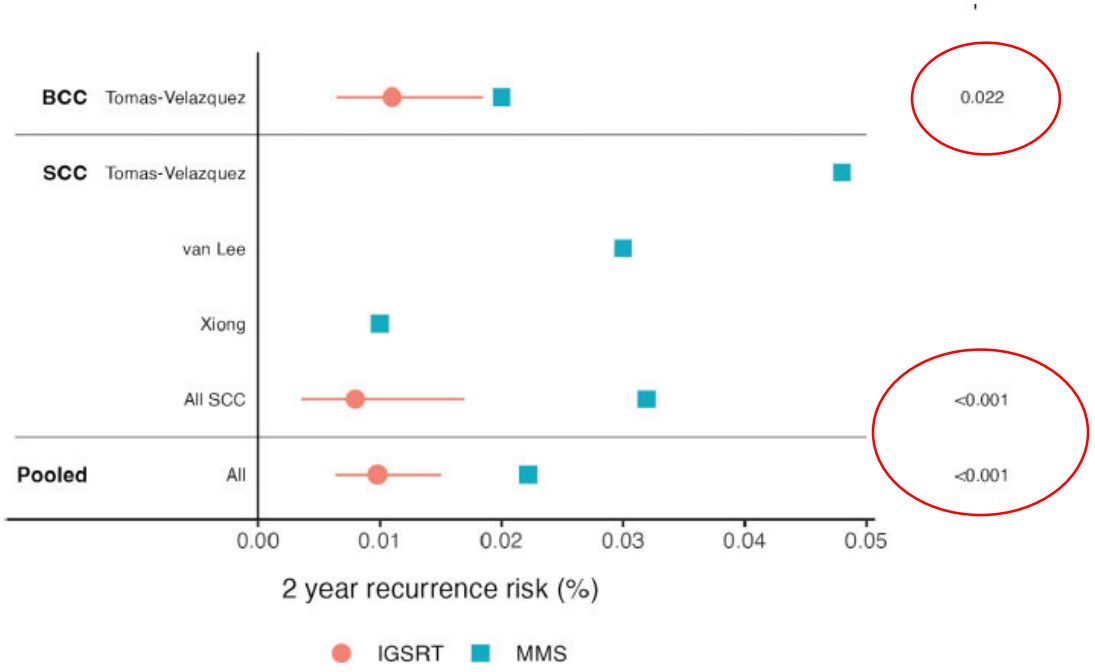
Yu et al. BMC Cancer (2023)

Radiothérapie de contact

Comparaison IGSRT et chirurgie

Summary of studies reporting the 2-year recurrence probabilities of SCCs and/or BCCs treated by MMS or IGSRT.

Authors, year	PMID	Disease	Study design	Treatment modality	Cohort (n/age/sex)	2-year recurrence probability
Alejandra Tomas-Velazquez, 2021	34,694,418	SCC, BCC	Prospective cohort conducted in 22 Spanish centers and a multivariate analysis	MMS	n = 371 SCC n = 4,402 BCC	0.048 for SCC 0.020 for BCC
C.B. van Lee, 2018	30,199,574	SCC	Retrospective multi-institution (2) cohort study	MMS	n = 380 262 men, 118 women median age 76 (IQR 69–81)	0.030
David D. Xiong, 2020 Erin McClure, 2022	31,887,322	SCC SCC, BCC	Retrospective single institution chart review Retrospective cohort study	MMS IGSRT	n = 238 BCC (N = 1382) SCC (N = 904)	0.010 BCC 0.011 SCC 0.008

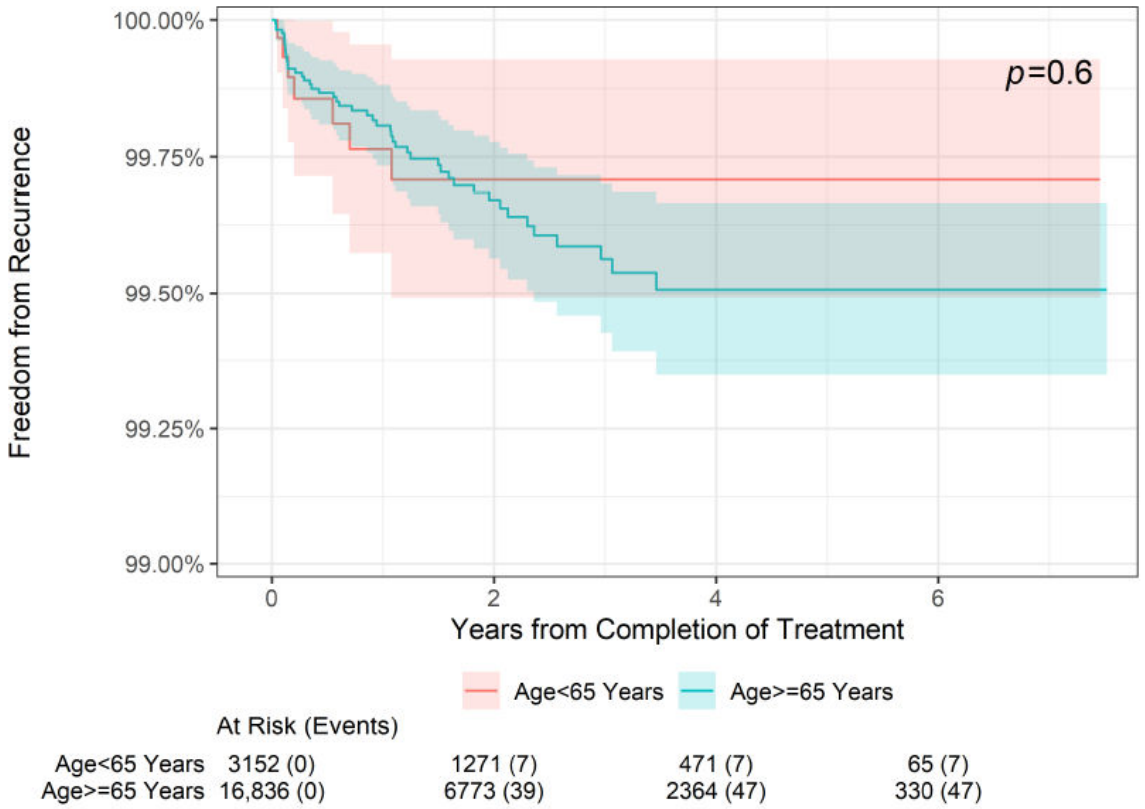


Taux de récidive à 2 ans supérieur en chirurgie de type mohs par rapport à l'IGSRT
Le chirurgien doit-il prendre sa retraite ?

EM Mc Clure et al. Clinical and Translational Radiation Oncology 43 (2023)

Radiothérapie de contact

Résultats selon différents paramètres



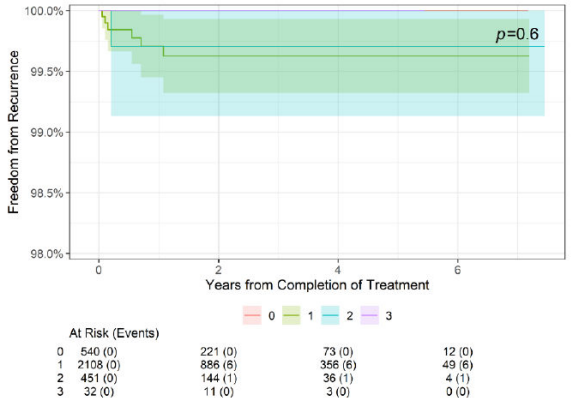


Figure 3. Two-year, four-year, and six-year freedom from recurrence over time of NMSC treated with IGSRT by stage among younger (age < 65 years) patients. AJCC 8th edition staging used.

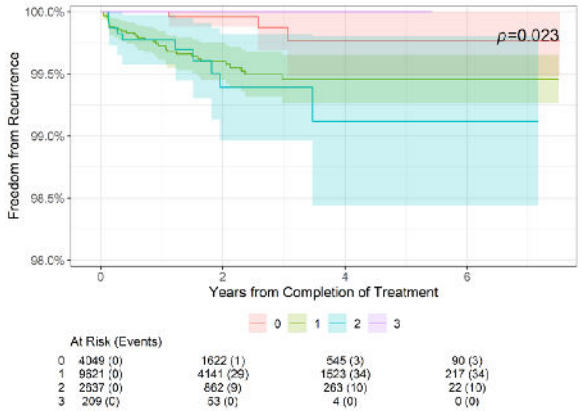


Figure 4. Two-year, four-year, and six-year freedom from recurrence over time of NMSC treated with IGSRT by stage among older (age ≥ 65 years) patients. AJCC 8th edition staging used.

IGSRT excellente alternative de première ligne pour les patients présentant une tumeur cutanée quelque-soit l'âge, le sexe , la classification selon AJCC

Farber et al. Geriatrics 2024

Radiothérapie externe de haute énergie

Résultats historiques

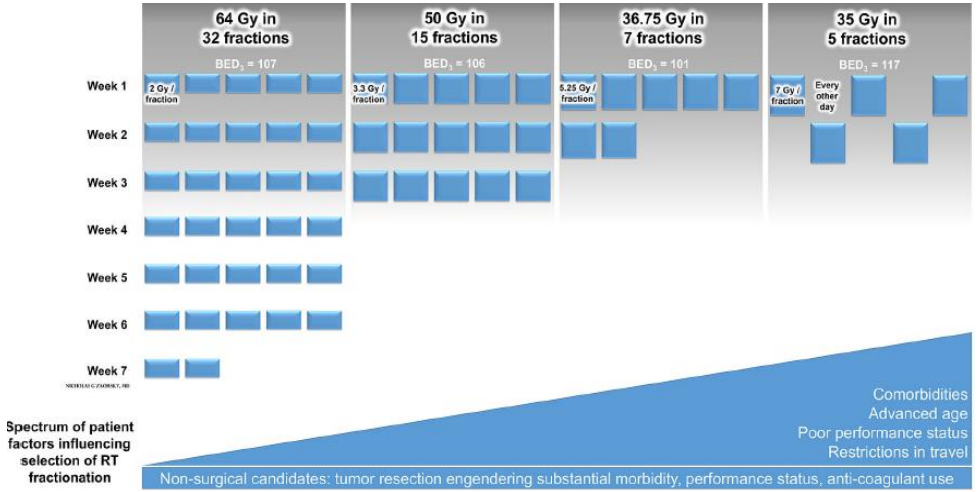
Author	Number of Patients	Pathology	Outcome	Complications	Radiotherapy Modality and Fractionation
Lee 1993 [28]	67	T4 BCC + SCC	5 years local control with radiotherapy—53% With salvage surgery 5 years—74%	9% severe complication	X-ray 250 kV—31.3% External beam—28.4% Megavoltage photons—25% Electron beam—12% Other modality—3%
Kwan 2004 [21]	182	T2 or higher BCC + SCC	4 years local control for BCC—86% 4 years local control for SCC—58%		Orthovoltage X-ray, electron beam, megavoltage photons
Locke 2001 [22]	65	T3/T4 BCC + SCC	5 years local control for BCC—85% 4 years local control for SCC—71%	5.8%	Soft X-ray (contact) radiotherapy—60% Electron beam radiotherapy—19% Soft X-ray and electron beam combination—20% Megavoltage—<2%
Al-Othman 2001 [29]	88	Stage 4 BCC + SCC	5 years local control with radiotherapy—53% With salvage surgery 5 years—90%	17% severe complication	External beam—87.5% Interventional radiotherapy (brachytherapy)—2.2% External beam with interventional radiotherapy (brachytherapy) boost—10.3%
Balamucki 2012 [32]	49	SCC with incidental PNI	RT 5 years local control—42% CRT 5 years local control—62%		No data regarding radiotherapy modality
Kim 2018 [36]	34	T3/T4 BCC + SCC	3 years DSS for BCC—93.3% 3 years DSS for SCC—38.3%		Orthovoltage photons Megavoltage photons Electron beam therapy Proton therapy
Hiura 2019 [37]	21	Stage 4 SCC	One year overall survival—79% One year progression-free survival—44%		Chemoradiotherapy—no specific radiation protocol described
Hazim 2021 [38]	21	SCC with clinical PNI	RT/CRT 2 years local control—59.8%	Dermatitis—67% Mucositis—57%	External beam radiotherapy—52% Proton therapy—48%

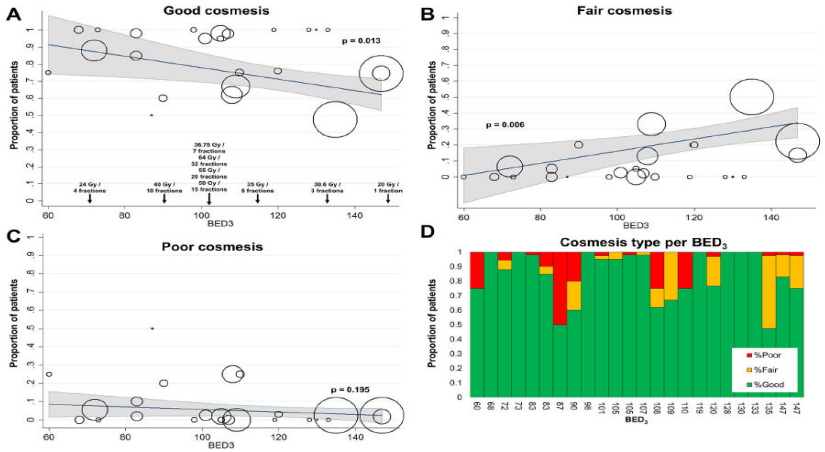
Réservé aux tumeurs évoluées: taux de contrôle local variant de 42 à 86%
Hétérogénéité des techniques et tumeurs

Yosefof et al. Cancer 2023

Radiothérapie externe de haute énergie

Hypofractionnement c'est possible





HIGHLIGHTS

- Clinicians are hesitant to use hypofractionated RT for indolent skin cancers.
- In this meta-analysis, we included 9,729 patients and used radiobiologic modeling to predict cosmesis with various fractionation regimens.
- We conclude that with hypofractionated RT, poor cosmesis is noted in <8% of patients, and local recurrence in <15%, independent of fractionation regimen used.
- We recommend clinicians consider these commonly-used regimens: 50 Gy / 15 fractions, 36.75 Gy / 7 fractions, or 35 Gy / 5 fractions, as they result in "good" cosmesis in 80% of patients.

Zaorsky et al. Radiot Oncol 2020

Radiothérapie externe de haute énergie

Radiothérapie adjuvante: pour les hauts-risques

TABLE 3 Recommendations and considerations for adjuvant therapy, immunotherapy, and targeted therapy for high-risk cSCC

Treatment	NCCN[7,78]	AAD[79]	ASTRO Task Force[40]
Radiation therapy	Recommends ART to primary site[a]: • for extensive PNI • with large (nerve caliber ≥0.1 mm) nerve involvement • when there are positive margins postsurgery	Recommends consideration of ART to primary site: • for concerning PNI • for high risk for regional or distant metastasis	Strongly recommends ART to primary site: • for clinically or radiologically apparent gross PNI • when further surgery cannot correct or close positive margins • when there is recurrence following a margin-negative resection • for T3 and T4 tumors (AJCC8) • for chronically immunosuppressed patients with desmoplastic or infiltrative tumors

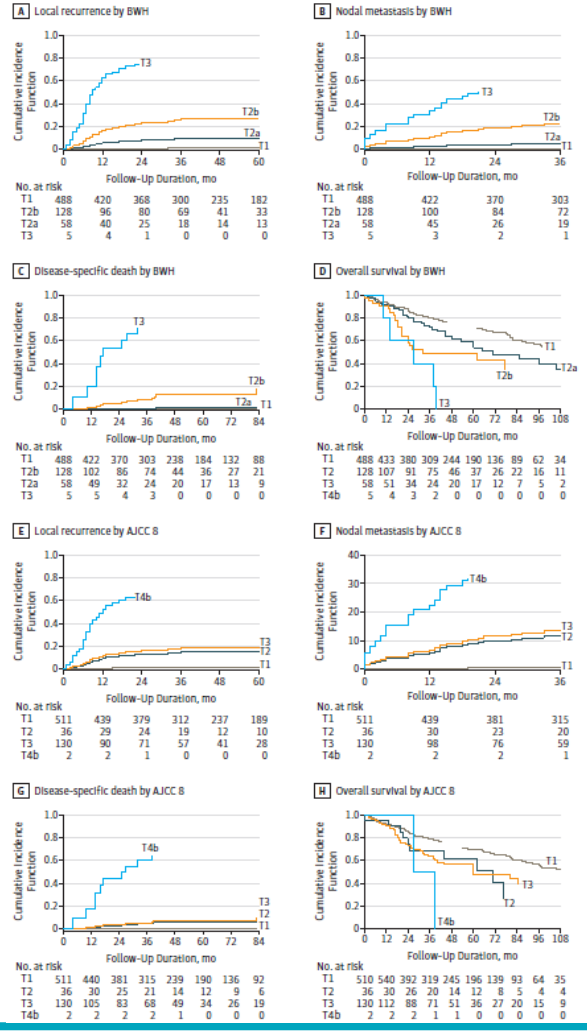
NCCN Guidelines[a]	One positive LN ≤3 cm, no ECE	Either ART or observation	ASTRO Task Force[b]	Clinically apparent regional LN metastasis following LN dissection (except when there is only one small [<3 cm] carcinoma-positive cervical LN, without ECE)	Strongly recommends ART for treating regional LNs	40
	Two or more positive LNs, no ECE	ART		LN basin overlap with primary site when patients are undergoing primary site RT (primary tumor >6 mm)	Elective ART is conditionally recommended for the LN basin	
	One positive LN >3 cm, no ECE	ART		High risk for regional LN involvement	SLNB and imaging are conditionally recommended to determine the need for ART	
	Incompletely excised LN disease	ART and consideration of concurrent adjuvant systemic therapy		Locally advanced disease	Strongly recommends against concurrent use of carboplatin with ART	
	One or more nodes with ECE	ART and consideration of concurrent adjuvant systemic therapy within a clinical trial				

Données discordantes sur les indications de radiothérapie adjuvante.
Comment sélectionner les patients ?

Newman et al. Head and Neck 2021

Radiothérapie externe de haute énergie

Radiothérapie adjuvante Comment sélectionner les hauts risques ?



Tumor Staging System	Definition
AJCC 8th Edition	
T1	<2 cm in greatest diameter
T2	≥2 cm, but <4 cm in greatest diameter
T3	Tumor ≥4 cm in greatest diameter or minor bone invasion or perineural invasion or deep invasion[a]
T4a	Tumor with gross cortical bone and/or marrow invasion
T4b	Tumor with skull bone invasion and/or skull base foramen involvement
BWH	
T1	0 High-risk factors[b]
T2a	1 High-risk factor
T2b	2-3 High-risk factors
T3	4 High-risk factors or bone invasion

[b] BWH high-risk factors include tumor diameter ≥2 cm, poorly differentiated histology, perineural invasion of nerve(s) ≥0.1 mm in caliber, or tumor invasion beyond subcutaneous fat (excluding bone invasion, which upgrades tumor to BWH stage T3).

Classification BWH permet de mieux sélectionner et isoler les patients à haut risque

Ruiz et al. JAMA Dermato 2019

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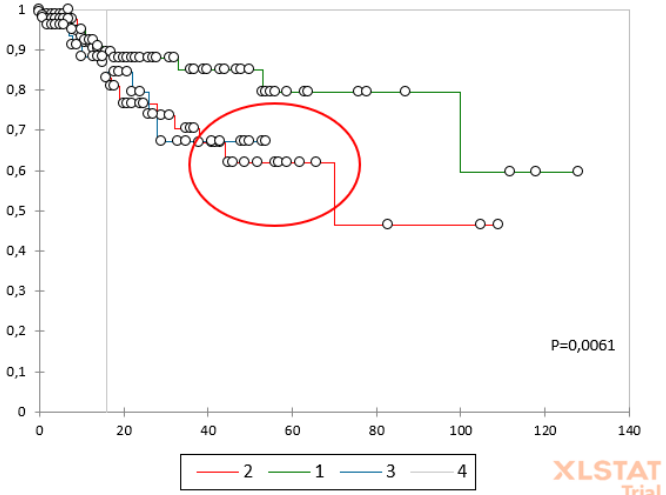
Survie Globale selon AJCC



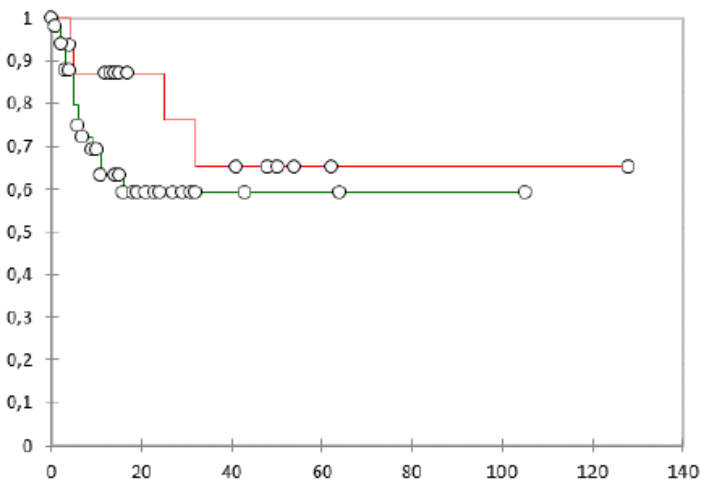


Figure 2A. DFS comparison beetween irradiated patients (red-line) and non irradiated patients (green-line) for T1and T2a patients according to BWH Classification

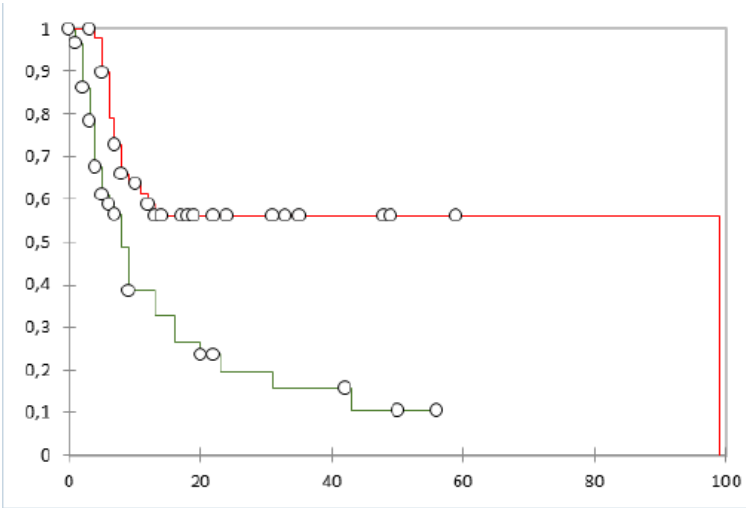
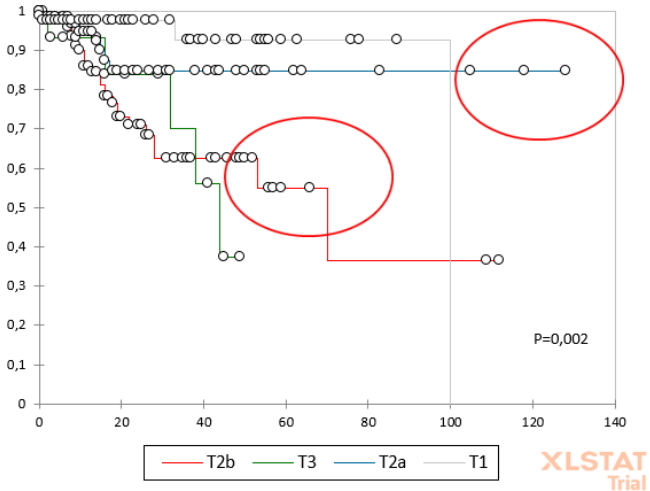


Figure 2B. DFS comparison beetween irradiated patients (red-line) and non irradiated patients (green-line) for T2B and T3 patients according to BWH Classification

Survie globale selon BWH



Net impact de la radiothérapie sur la survie sans récidive a partir des lésions classées T2B BWH

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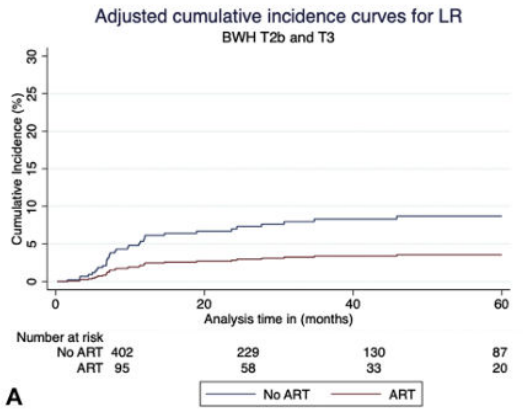
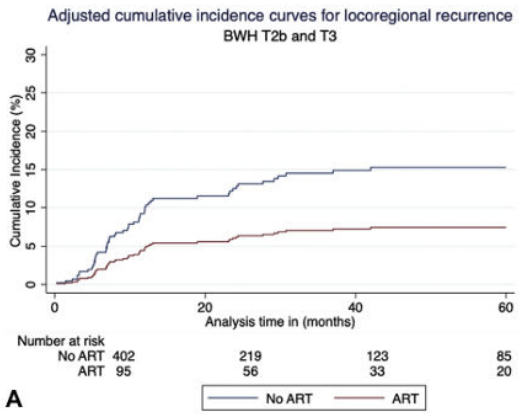
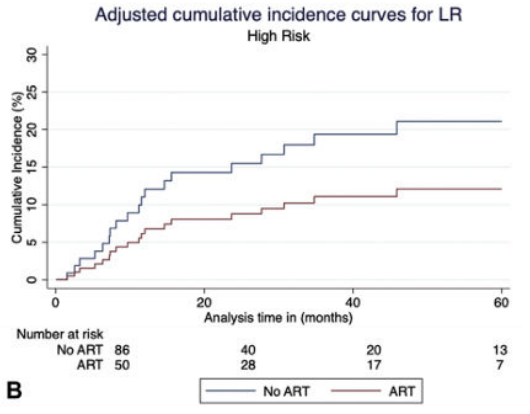






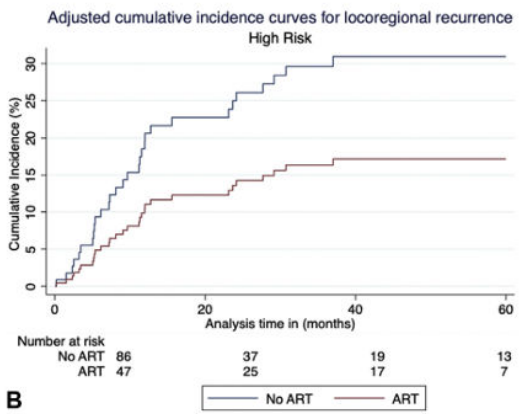


Table III. Five-year cumulative incidences for local recurrence, metastasis, and disease-specific death for BWH T2b and BWH T3 tumors with negative surgical margins

	5-y cumulative incidence, % (95% CI)	
	BWH T2b and T3 tumors	
	ART$^-$	ART$^+$
Locoregional recurrence	15.3 (11.9-22.1)	7.5 (4.4-11.9)
Local recurrence	8.7 (6.3-12.0)	3.6 (1.6-7.7)
Regional recurrence	8.8 (6.2-13.4)	4.9 (2.1-11.3)
Disease-specific death	6.0 (4.2-11.3)	6.2 (3.8-15.5)
	High-risk tumors	
	ART$^-$	ART$^+$
Locoregional recurrence	31.0 (26.1-40.8)	17.2 (11.9-26.4)
Local recurrence	21.1 (12.5-33.6)	12.1 (5.2-27.0)
Regional recurrence	12.1 (6.6-21.5)	3.0 (0.8-11.2)
Disease-specific death	16.5 (10.3-26.2)	16.1 (9.9-25.5)
	Low-risk tumors	
	ART$^-$	ART$^+$
Locoregional recurrence	11.8 (7.7-16.2)	7.1 (4.8-10.8)
Local recurrence	0	0
Regional recurrence	7.8 (5.2-11.7)	5.3 (1.7-15.3)
Disease-specific death	4.5 (3.0-8.3)	7.7 (4.5-18.4)

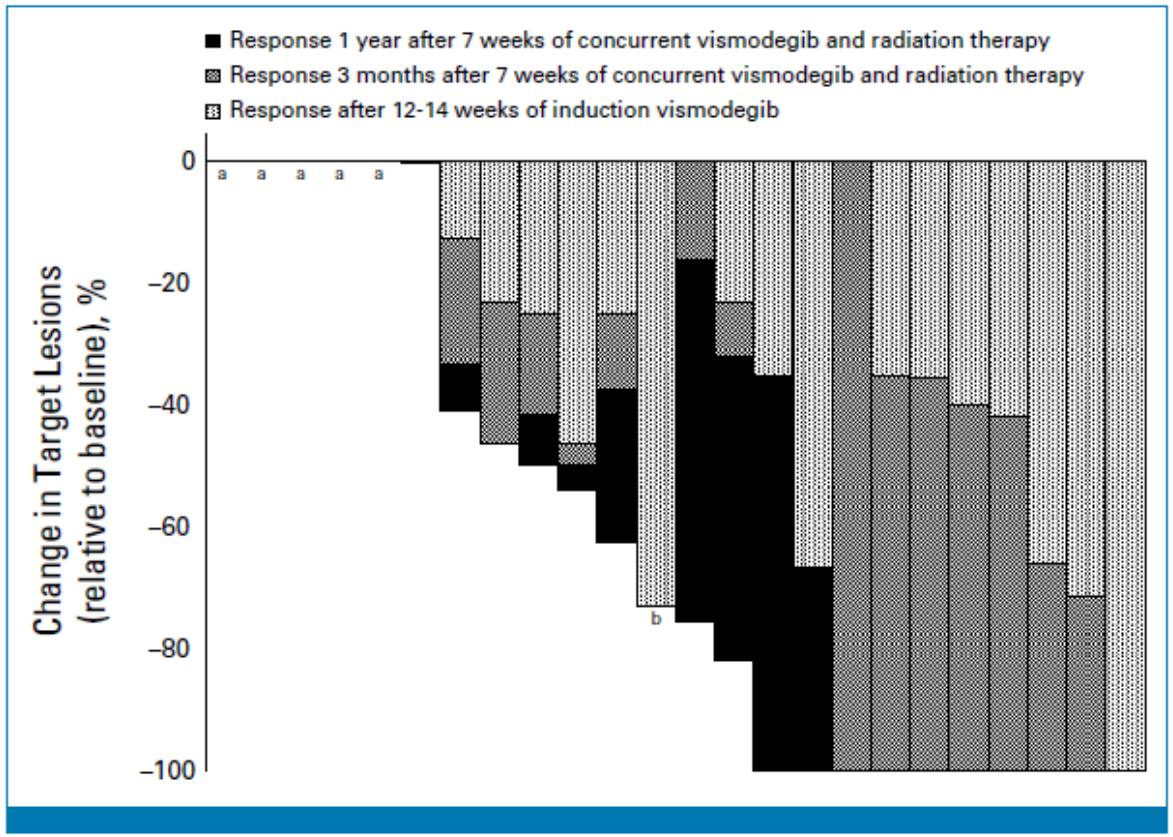
ART, Adjuvant radiation; *BWH*, Brigham and Women's Hospital.

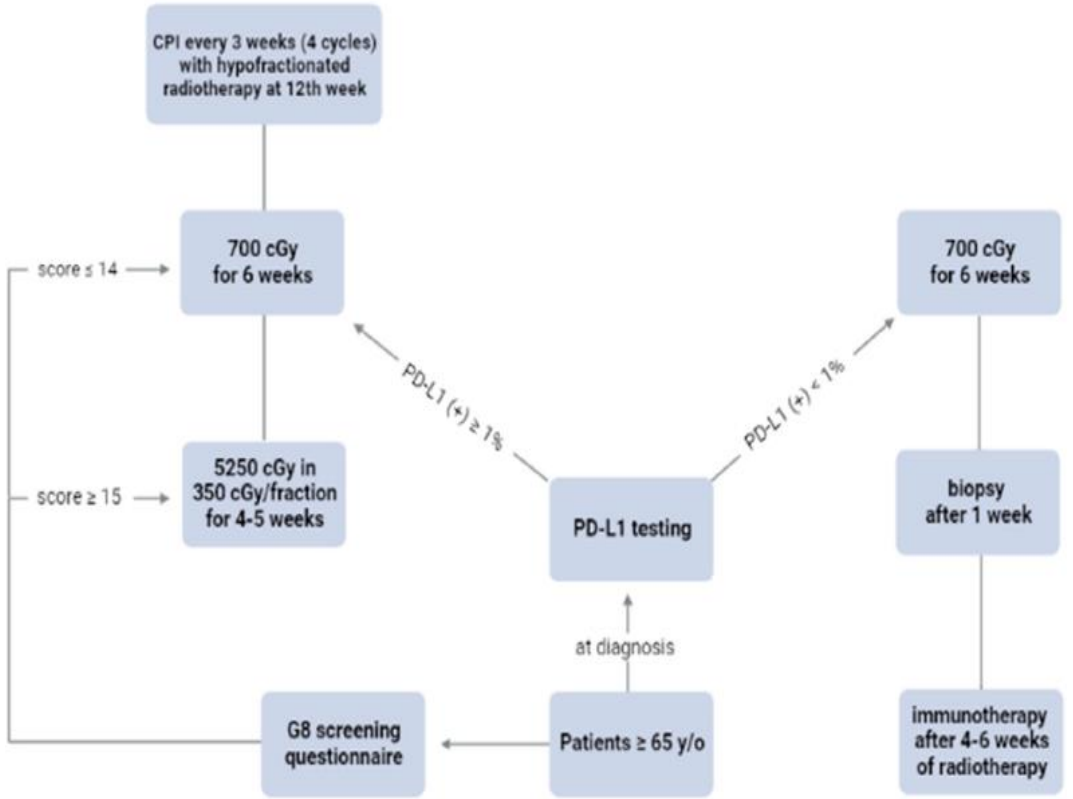
Résultats identiques autre équipe: Classification idéale pour sélectionner les patients devant bénéficier d'une radiothérpaie adjuvante?

Ruiz et al. J AM Acad Dematol 2022

Radiothérapie externe de haute énergie

Perspectives: associations





RT et VISMODEGIB : bon profil de réponse et de toxicité

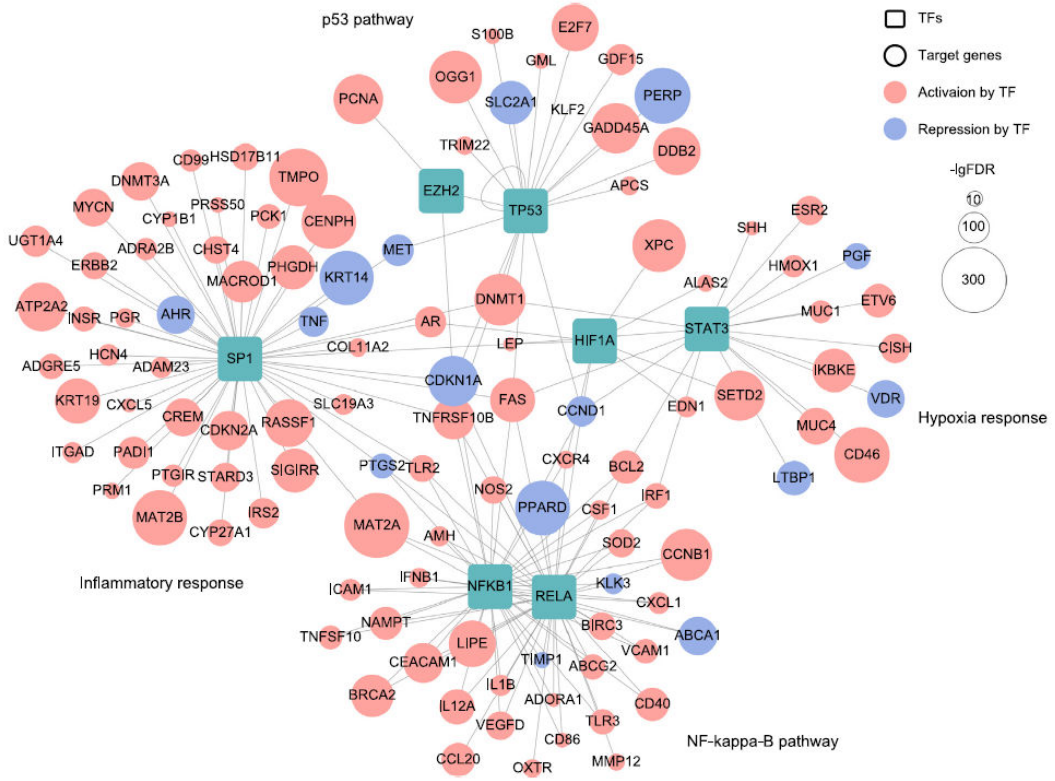
Association avec l'immunothérapie pour les CEC

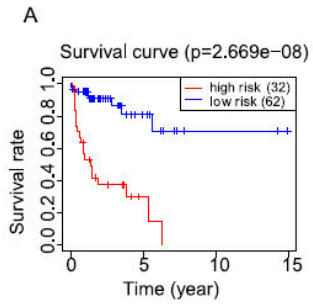
Barker et al. JCO 2024

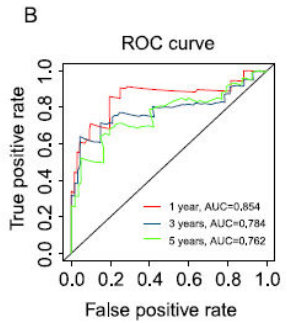
Nguyen et al. Cancer 2023

Radiothérapie externe de haute énergie

Perspectives: Signature génomique







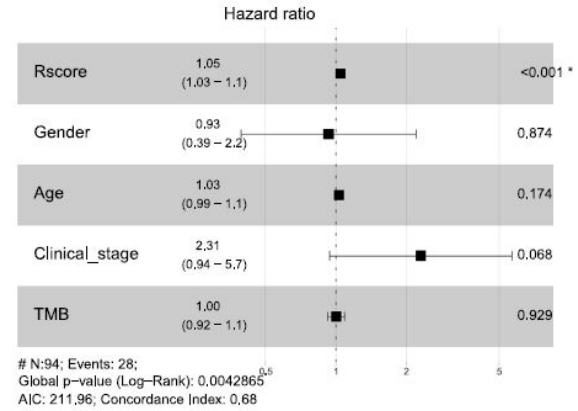


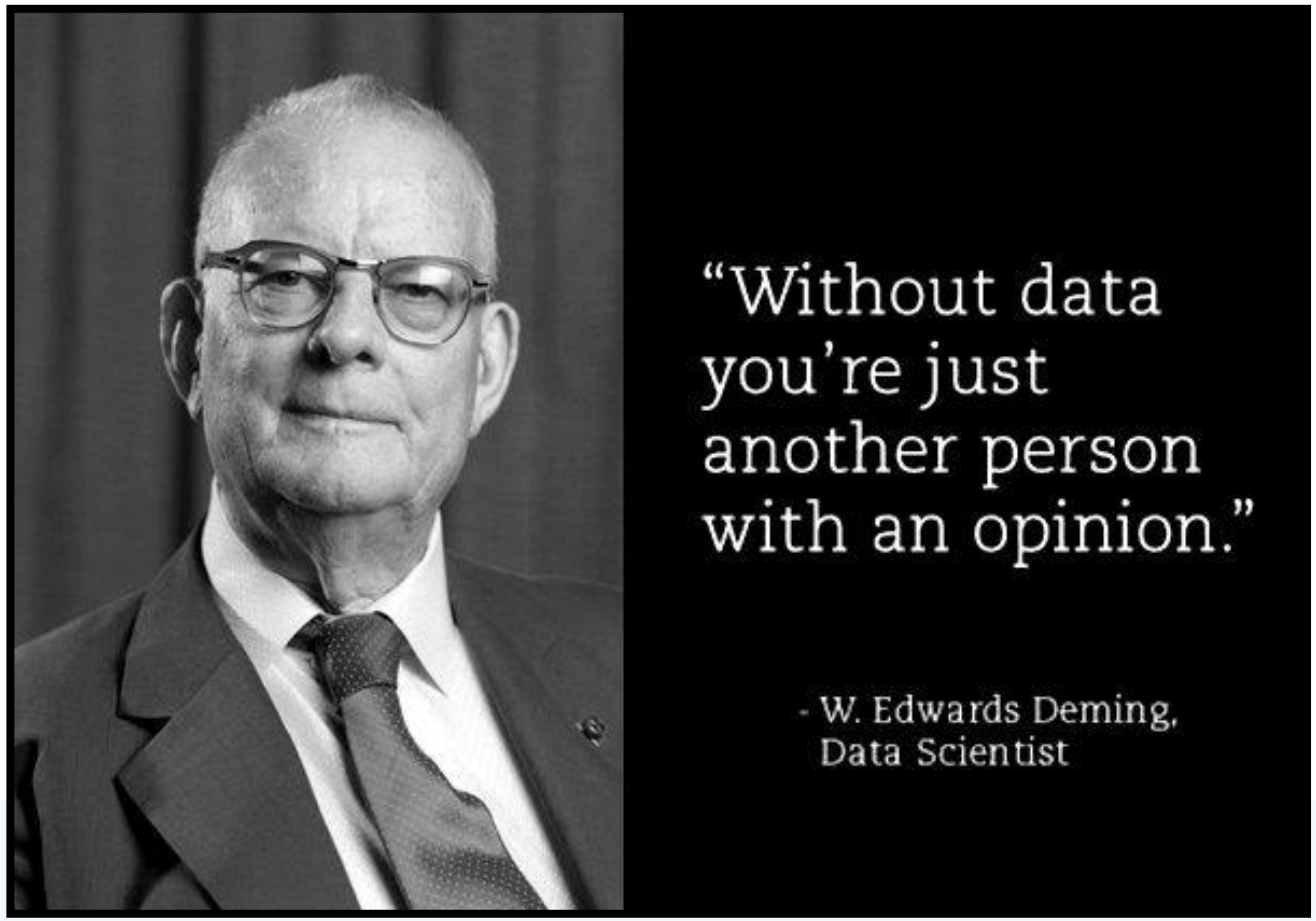
Fig. 6. Significantly activated transcription factors and their target differentially expressed genes in the radioresistant tumours compared with the radiosensitive tumours.

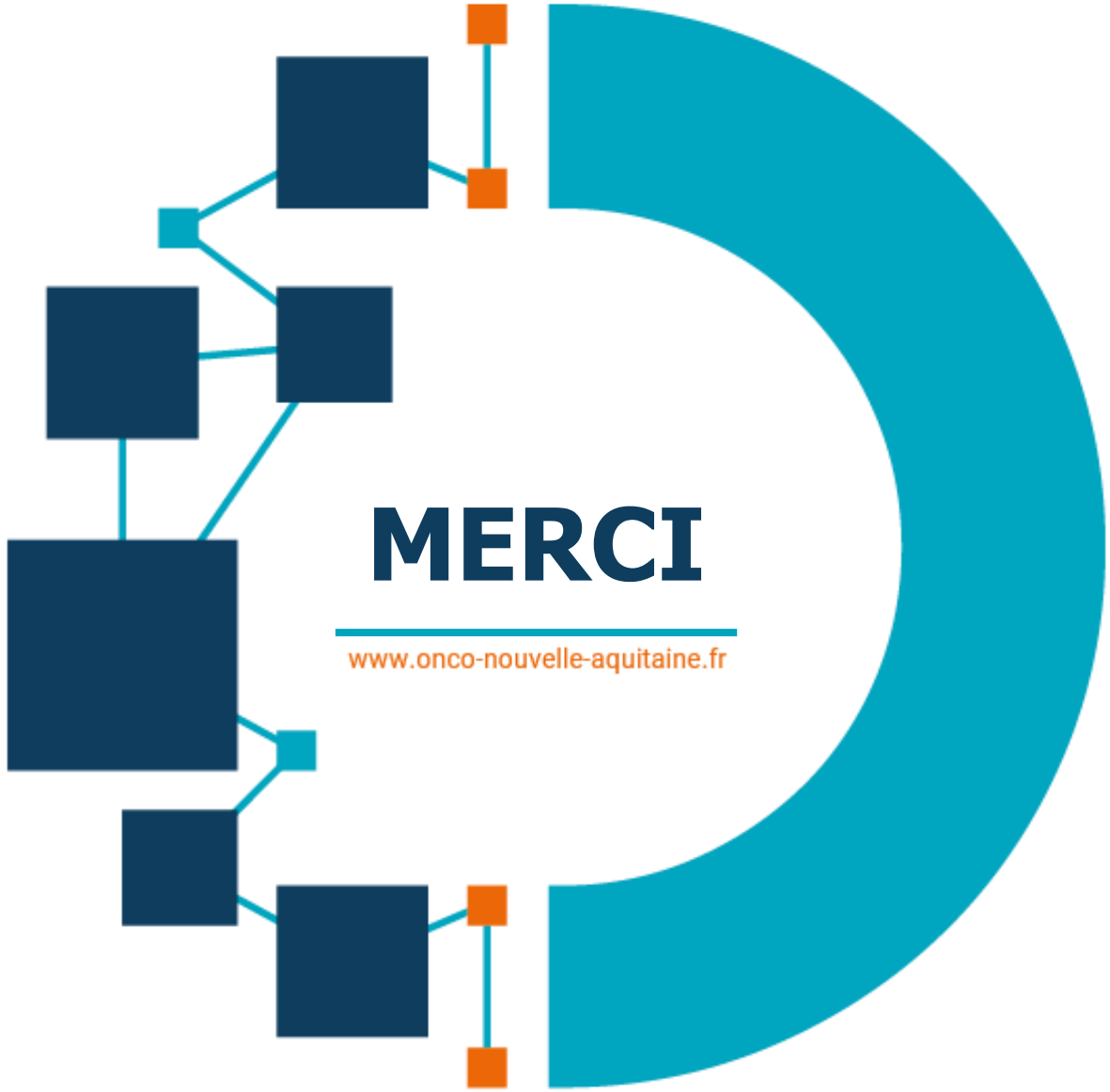
Signature génomique sur 13 gènes pour déterminer les lésions à haut risque de radiorésistance diminuée (association de traitement nécessaire)

Li et al. Radioth Oncol 2021

CONCLUSION

Merci pour votre attention

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