

Procédures cliniques en radio- oncologie

Tumeurs de la sphère ORL

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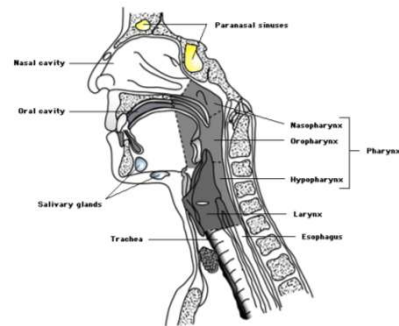
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Les cancers ORL

- Classiquement, carcinomes épidermoïdes des muqueuses de la cavité buccale ou du pharynx
- Inclut également des tumeurs plus rares des:
 - Glandes salivaires
 - Sinus
 - Carcinomes épidermoïdes cutanées de la tête et du cou
 - Cas particulier = lymphomes, traité comme les autres lymphomes

Cancers ORL – classification

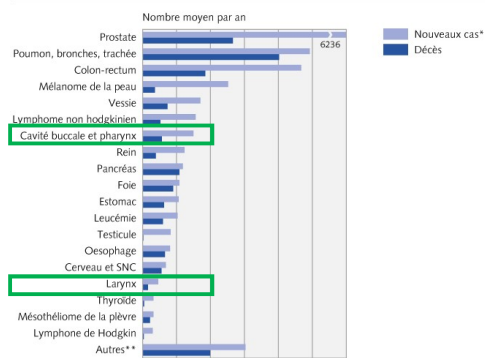
- Nasopharynx
- Oropharynx
- Cavité buccale
- Hypopharynx
- Larynx



Stadification et stratégies différentes selon la localisation

Incidence en Suisse

Nouveaux cas et décès chez les hommes selon la localisation cancéreuse, 2008–2012

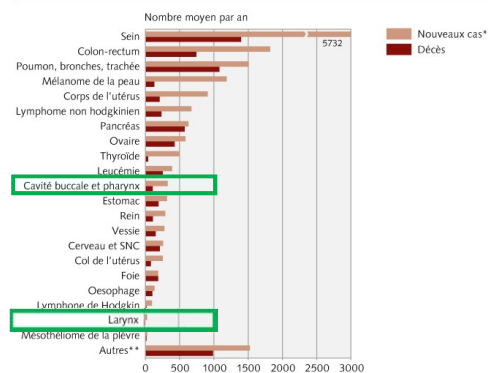


* Nouveaux cas estimés sur la base des données des registres des tumeurs
** Nouveaux cas sans les cancers non mélaniques de la peau

Source: Le cancer en Suisse, rapport 2015, graphique G 3.1

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Nouveaux cas et décès chez les femmes selon la localisation cancéreuse, 2008–2012

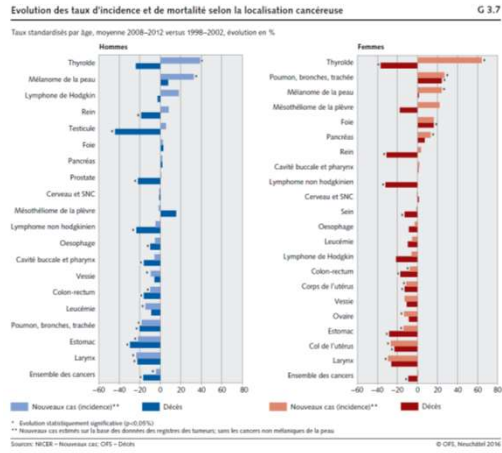


* Nouveaux cas estimés sur la base des données des registres des tumeurs
** Nouveaux cas sans les cancers non mélaniques de la peau

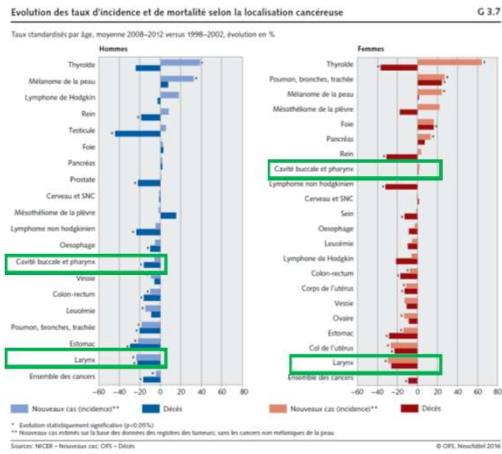
Source: Le cancer en Suisse, rapport 2015, graphique G 3.1

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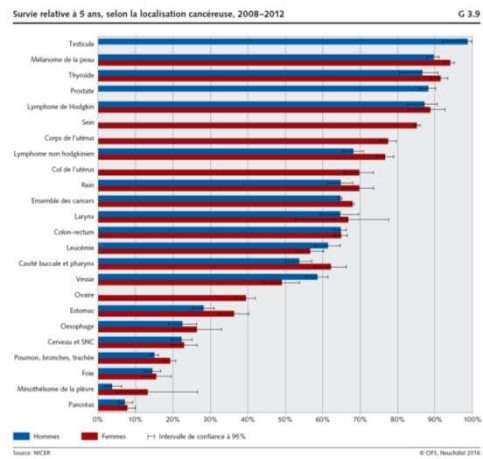
Tendances en Suisse



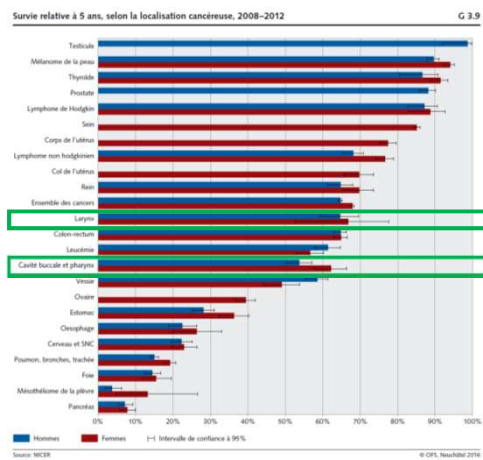
Tendances en Suisse



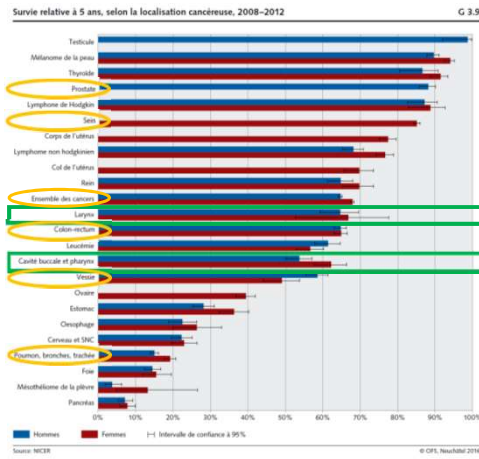
Pronostic



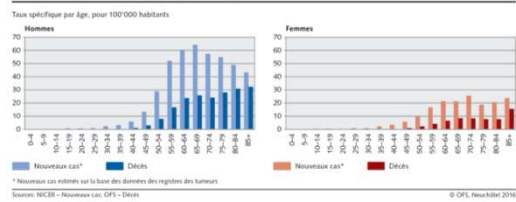
Pronostic



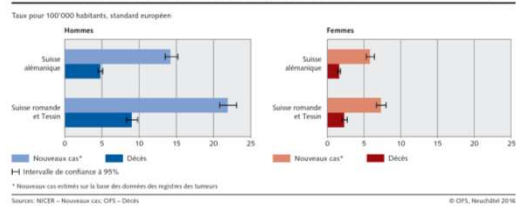
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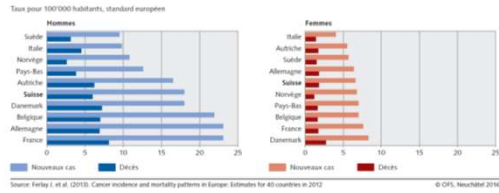
Cancer de la cavité buccale et du pharynx selon l'âge, 2008-2012 G 4.1.1



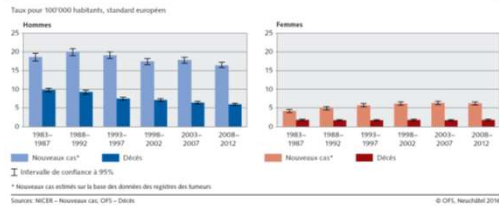
Cancer de la cavité buccale et du pharynx: comparaison régionale, 2008-2012 G 4.1.2



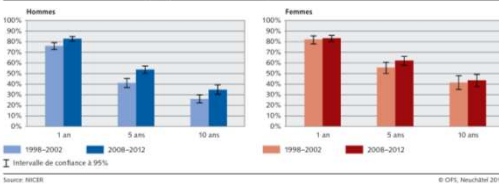
Cancer de la cavité buccale et du pharynx: comparaison internationale, 2012 G 4.1.3



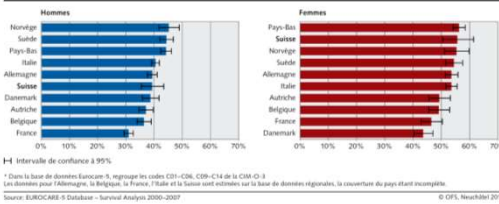
Cancer de la cavité buccale et du pharynx: évolution temporelle G 4.1.4



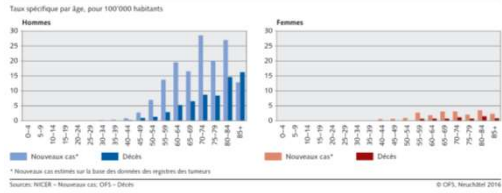
Cancer de la cavité buccale et du pharynx: survie relative à 1, 5 et 10 ans G 4.1.5



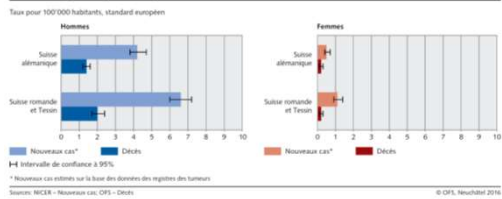
Cancer de la cavité buccale et du pharynx*: comparaison internationale de la survie relative à 5 ans, 2000-2007 G 4.1.6



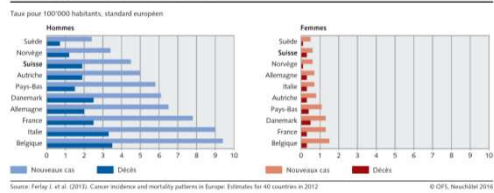
Cancer du larynx selon l'âge, 2008-2012 G 4.7.1



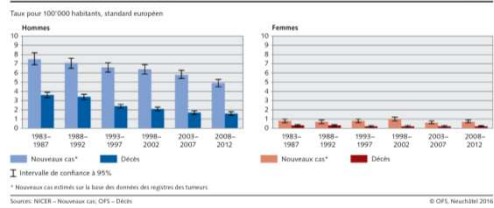
Cancer du larynx: comparaison régionale, 2008-2012 G 4.7.2



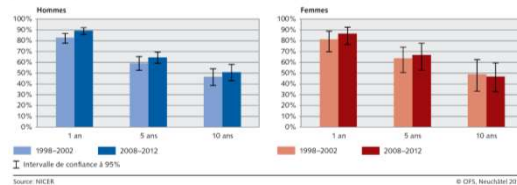
Cancer du larynx: comparaison internationale, 2012 G 4.7.3



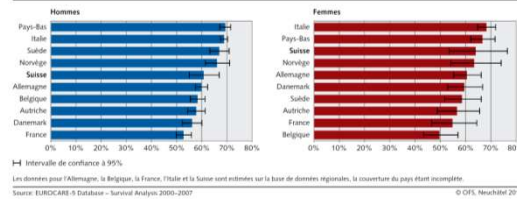
Cancer du larynx: évolution temporelle G 4.7.4



Cancer du larynx: survie relative à 1, 5 et 10 ans G 4.7.5



Cancer du larynx: comparaison internationale de la survie relative à 5 ans, 2000-2007 G 4.7.6



Facteurs de risque

- Classiquement (environ $\frac{3}{4}$ des cas actuellement):
 - Tabac (fumé ou mastiqué)
 - OH
- Autres majeurs (environ $\frac{1}{4}$ des cas, en progression):
 - EBV (Epstein-Barr virus) dans les cancers du nasopharynx
 - HPV (human papilloma virus) dans les cancers de l'oropharynx
- Plus rares:
 - Expositions professionnelles (sciure, formaldéhyde)
 - Saumure, reflux, mauvaise hygiène buccale, etc...
- Pas de vraie rôle d'une prédisposition génétique

Facteurs de risque

- Classiquement (environ $\frac{3}{4}$ des cas actuellement):
 - Tabac
 - OH
- Autres majeurs (environ $\frac{1}{4}$ des cas, **en progression**):
 - EBV (Epstein-Barr virus) dans les cancers du nasopharynx
 - **HPV (human papilloma virus) dans les cancers de l'oropharynx**
- Plus rares:
 - Poussières de bois dans des tumeurs rares des sinus (esthésioneuroblastome)
 - ...
- Pas de vraie rôle d'une prédisposition génétique

HPV - rappel

Plan de vaccination suisse											
Vaccinations de base						Vaccinations complémentaires					
Age	DTP ^a	Polio	Hib	HBV	ROR	HPV ^b	Varicelle	Grippe	Pneumocoques	Méningocoques	HPV ^c
2 mois	DTP ^a	IPV	Hib	(HBV)					PCV		
4 mois	DTP ^a	IPV	Hib	(HBV)					PCV		
6 mois	DTP ^a	IPV	Hib	(HBV)							
12 mois					ROR				PCV		
12-15 mois										MCV-C	
15-24 mois	DTP ^a	IPV	Hib	(HBV)	ROR						
4-7 ans	DTP ^a	IPV			✓						
11-14/15 ans	dTp ^a	✓		HBV	✓	HPV ^b	VZV			MCV-C	HPV ^c
25-29 ans	dTp ^a	✓		✓	✓		✓				HPV
45 ans	dT	✓		✓	✓						
≥ 65 ans	dT							Grippe			

✓ Vérifier que les vaccinations soient complètes: si ce n'est pas le cas, procéder au rattrapage vaccinal.

HPV - rappel

Plan de vaccination suisse

Age	Vaccinations de base					Vaccinations complémentaires					
	DTP*	Polio	Hib	HBV	ROR	HPV	Varicelle	Grippe	Pneumocoques	Méningocoques	HPV
2 mois	DTP*	IPV	Hib	(HBV)					PCV		
4 mois	DTP*	IPV	Hib	(HBV)					PCV		
6 mois	DTP*	IPV	Hib	(HBV)							
12 mois					ROR				PCV		
12-15 mois										MCV-C	
15-24 mois	DTP*	IPV	Hib	(HBV)	ROR						
4-7 ans	DTP*	IPV			✓						
11-14/15 ans	dTp*	✓		HBV	✓	HPV♂	VZV			MCV-C	HPV♀
25-29 ans	dTp*	✓		✓			✓				HPV
45 ans	dT	✓		✓	✓						
≥ 65 ans	dT						Grippe				

✓ Vérifier que les vaccinations soient complètes: si ce n'est pas le cas, procéder au rattrapage vaccinal.

HPV - rappel

Maladies transmissibles

Vaccination contre les HPV: recommandation de vaccination complémentaire pour les garçons et jeunes hommes âgés de 11 à 26 ans

Depuis 2007, la vaccination contre les papillomavirus humains (HPV) est recommandée en Suisse pour toutes les filles et les jeunes femmes à titre de vaccination de base afin de prévenir le développement du cancer du col de l'utérus et d'autres maladies provoquées par les HPV. Sur la base des dernières connaissances scientifiques, l'OFSP et la CFV recommandent aujourd'hui d'étendre la vaccination aux garçons et aux jeunes hommes âgés de 11 à 26 ans, de préférence entre 11 et 14 ans, avant le début de l'activité sexuelle. Cette vaccination est recommandée à titre de vaccination complémentaire pour la prévention des cancers et des verrues génitales associés aux HPV.

ment de la néoplasie [5;9-12]. Plus de 80 % des cancers de l'anus sont causés spécifiquement par les HPV de types 16 et 18, dont les antigènes sont contenus dans les vaccins [9;12;13]. Le tableau 1 ci-dessous montre quels pourcentages de ces cancers sont associés aux HPV16/18.

Le poids total des tumeurs associées aux HPV chez les hommes et les femmes est estimé à environ 5 % de l'ensemble des cancers dans le monde, celui qui pèse sur les femmes étant toutefois le plus important [12]. Certaines données font état d'une augmentation de l'incidence des tumeurs induites par les HPV chez les deux sexes [14-16].

HPV - rappel

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HPV - rappel

Tableau 1

Nombre moyen de cas et taux d'incidence (pour 100 000 personnes-années, standardisé sur l'âge) de nouveaux diagnostics de cancer en Suisse (période: 2007-2011, NICER [17]) et proportion des cas de cancer induits par les HPV16/18 (estimation sur la base de données recueillies à l'échelle internationale [9;12]). En raison du faible nombre de cas, le NICER ne publie pas de données sur les cancers du pénis, de la vulve et du vagin.

	Hommes	Femmes
Oropharynx, amygdales, base de la langue (ICD-10 C01, C09-10)	274 cas/année ^a Incidence: 6,2/100 000 ^a HPV16/18: 12-50 % ^c	92 cas/année ^a Incidence: 1,9/100 000 ^a HPV16/18: 12-50 % ^c
Anus et canal anal (ICD-10 C21)	57 cas/année ^b Incidence: 1,2/100 000 ^b HPV16/18: 81 % ^c	121 cas/année ^b Incidence: 2,3/100 000 ^b HPV16/18: 81 % ^c
Cervix (ICD-10 C53)		252 cas/année ^b Incidence: 5,3/100 000 ^b HPV16/18: >70 % ^c
Total	331 cas/année	465 cas/année
Total des cas associés aux HPV16/18 et donc théoriquement évitables par la vaccination	79-183 cas/année	285-320 cas/année

HPV - rappel

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Nombre moyen de cas et taux d'incidence (pour 100 000 personnes-années, standardisé sur l'âge) de nouveaux diagnostics de cancer en Suisse (période: 2007-2011, NICER [17]) et proportion des cas de cancer induits par les HPV16/18 (estimation sur la base de données recueillies à l'échelle internationale [9;12]). En raison du faible nombre de cas, le NICER ne publie pas de données sur les cancers du pénis, de la vulve et du vagin.

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Total	331 cas/année	485 cas/année
Total des cas associés aux HPV16/18 et donc théoriquement évitables par la vaccination	79-183 cas/année	285-320 cas/année

Les cancers ORL liés à l'HPV

- Cancers HPV+ de plus en plus fréquents, mais heureusement de meilleur pronostic
- D'où actuellement de multiples études en cours cherchant à «désescalader» les traitements de ces cancers en ORL, via:
 - Moins (ou pas) de chimio
 - Moins (ou pas) de RT
 - Doses moins élevées
 - Volumes moins étendus

Présentation clinique

- Douleurs pharyngées ou buccales (ou parfois référées au niveau de l'oreille)
- Masse dans la gorge/bouche ou dans le cou (adénopathies)
- Modification de la voix
- Fausses-routes
- Parésies ou pertes de sensibilité dans la région ORL ou de la face
- Perte de poids
- Obstruction nasale
- Etc...

Investigations cliniques

- Examen sphère ORL et cou
- Nasofibroscope
- Biopsie tumeur +/- ganglions suspects
 - Cas spécial = adénopathie «sans porte d'entrée» (unknown primary) → examen cutané, biopsies dirigées par la radiologie ou parfois à l'aveugle de la base de langue et amygdalectomie bilatérale

Bilan d'extension

- Panendoscopie (recherche tumeur synchrone bronches ou œsophage)
- Radiologie = en général:
 - IRM, pour l'extension locale et atteinte ganglionnaire
 - PET-CT (ou CT thoraco-abdominal), pour l'atteinte régionale ou à distance
 - Pas forcément de bilan poussé pour une tumeur précoce du larynx
- Les cancers ORL sont de façon général très lymphophiles, avec des atteintes métastatiques ganglionnaires fréquentes
- Atteintes à distance moins fréquentes (mais cancers synchrones p. ex. du poumon c/o le patient tabagique classique)

Staging selon TNM

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NCCN Guidelines Version 1.2021
Head and Neck Cancers

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Table 3
American Joint Committee on Cancer (AJCC)
TNM Staging System for the Oropharynx (p16-) and Hypopharynx (8th ed., 2017)
(Not included: P16-positive oropharyngeal cancers and nasopharyngeal cancer)

Oropharynx (p16-)	Hypopharynx
TX Primary tumor cannot be assessed	TX Primary tumor cannot be assessed
Tis Carcinoma in situ	Tis Carcinoma in situ
T1 Tumor 2 cm or smaller in greatest dimension	T1 Tumor limited to one subsite of hypopharynx and/or 2 cm or smaller in greatest dimension
T2 Tumor larger than 2 cm but not larger than 4 cm in greatest dimension	T2 Tumor invades more than one subsite of hypopharynx or an adjacent site, or measures larger than 2 cm but not larger than 4 cm in greatest dimension without fixation of hemilarynx
T3 Tumor larger than 4 cm in greatest dimension or extension to lingual surface of epiglottis	T3 Tumor larger than 4 cm in greatest dimension or with fixation of hemilarynx or extension to esophageal mucosa
T4 Moderately advanced or very advanced local disease	T4 Moderately advanced or very advanced local disease
T4a Tumor invades the larynx, extrinsic muscle of tongue, medial pterygoid, hard palate, or mandible	T4a Tumor invades thyroid/cricoid cartilage, hyoid bone, thyroid gland, esophageal muscle or central compartment soft tissue
T4b Very advanced local disease	T4b Very advanced local disease
Tumor invades lateral pterygoid muscle, pterygoid plates, lateral hypopharynx, or skull base or encases carotid artery	Tumor invades prevertebral fascia, encases carotid artery, or involves mediastinal structures

Note: Mucosal extension to lingual surface of epiglottis from primary tumors of the base of the tongue and vallecula does not constitute invasion of the larynx.

Note: Central compartment soft tissue includes prelaryngeal strap muscles and subcutaneous fat.

[Continued](#)

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Table 3 — Continued
American Joint Committee on Cancer (AJCC)
TNM Staging System for the Oropharynx (p16-) and Hypopharynx (8th ed., 2017)
 (Not included: P16-positive (p16+) oropharyngeal cancers and nasopharyngeal cancer)

Regional Lymph Nodes (N)
Clinical N (cN) - Oropharynx (p16-) and Hypopharynx

N0 No regional lymph node metastasis

N1 Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension and ENE(-)

N2 Metastasis in a single ipsilateral node larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(-); or metastases in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(-); or in bilateral or contralateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(-)

N2a Metastasis in a single ipsilateral node larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(-)

N2b Metastases in multiple ipsilateral nodes, none larger than 6 cm in greatest dimension and ENE(-)

N2c Metastases in bilateral or contralateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(-)

N3 Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(-); or metastases in any nodes) and clinically overt ENE(+)

N3a Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(-)

N3b Metastases in any node(s) and clinically overt ENE(+)

Note: A designation of "U" or "L" may be used for any N category to indicate metastasis above the lower border of the cricoid (U) or below the lower border of the cricoid (L). Similarly, clinical and pathological ENE should be recorded as ENE(-) or ENE(+).

[Continued](#)

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Table 3 — Continued
American Joint Committee on Cancer (AJCC)
TNM Staging System for the Oropharynx (p16-) and Hypopharynx (8th ed., 2017)
 (Not included: P16-positive (p16+) oropharyngeal cancers and nasopharyngeal cancer)

Regional Lymph Nodes (N):
Pathological N (pN) - Oropharynx (p16-) and Hypopharynx

N0 No regional lymph node metastasis

N1 Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension and ENE(-)

N2 Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension and ENE(-); or larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(-); or metastases in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(-); or in bilateral or contralateral lymph node(s), none larger than 6 cm in greatest dimension and ENE(-)

N2a Metastasis in single ipsilateral node 3 cm or smaller in greatest dimension and ENE(-); or a single ipsilateral node larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(-)

N2b Metastases in multiple ipsilateral nodes, none larger than 6 cm in greatest dimension and ENE(-)

N2c Metastases in bilateral or contralateral lymph node(s), none larger than 6 cm in greatest dimension and ENE(-)

N3 Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(-); or in a single ipsilateral node larger than 3 cm in greatest dimension and ENE(-); or multiple ipsilateral, contralateral or bilateral nodes, any with ENE(+)

N3a Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(-)

N3b Metastases in a single ipsilateral node larger than 3 cm in greatest dimension and ENE(-); or multiple ipsilateral, contralateral or bilateral nodes, any with ENE(+)

N3c Metastases in any size and ENE(+)

Note: A designation of "U" or "L" may be used for any N category to indicate metastasis above the lower border of the cricoid (U) or below the lower border of the cricoid (L). Similarly, clinical and pathological ENE should be recorded as ENE(-) or ENE(+).

Distant Metastasis (M)
M0 No distant metastasis
M1 Distant metastasis

Histologic Grade (G)
GX Grade cannot be assessed
G1 Well differentiated
G2 Moderately differentiated
G3 Poorly differentiated
G4 Undifferentiated

Prognostic Stage Groups

Stage	T	N	M
Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1	N1	M0
	T2	N1	M0
	T3	N1	M0
Stage IVA	T1	N2	M0
	T2	N2	M0
	T3	N2	M0
Stage IVB	T4a	N0, N1, N2	M0
	Any T	Any N	M0
Stage IVC	Any T	Any N	M1

[Continued](#)

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Staging selon TNM

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Table 4
American Joint Committee on Cancer (AJCC) TNM Staging System for HPV-Mediated (p16+) Oropharyngeal Cancer (8th ed., 2017)
(Not including P16-negative oropharyngeal cancer)

Primary Tumor (T)	Prognostic Stage Groups
T0 No primary identified	Clinical
T1 Tumor 2 cm or smaller in greatest dimension	Stage I T0, T1, T2 NO, N1 MO
T2 Tumor larger than 2 cm but not larger than 4 cm in greatest dimension	Stage II T0, T1, T2 N2 MO
T3 Tumor larger than 4 cm in greatest dimension or extension to lingual surface of epiglottis	Stage III T3 N0, N1, N2 MO
T4 Moderately advanced local disease Tumor invades the larynx, extrinsic muscle of tongue, medial pterygoid, hard palate, or mandible or beyond*	Stage III T0, T1, T2, T3 N3 MO
Mucosal extension to lingual surface of epiglottis from primary tumors of the base of the tongue and vallecula does not constitute invasion of the larynx.	Stage IV T4 NO, N1, N2, N3 MO
	Stage IV Any T Any N M1
Regional Lymph Nodes (N)	Pathological
Clinical N (cN)	Stage I T0, T1, T2 NO, N1 MO
NX Regional lymph nodes cannot be assessed	Stage II T0, T1, T2 N2 MO
N0 No regional lymph node metastasis	Stage III T3, T4 NO, N1 MO
N1 One or more ipsilateral lymph nodes, none larger than 6 cm	Stage III T3, T4 N2 MO
N2 Contralateral or bilateral lymph nodes, none larger than 6 cm	Stage IV Any T Any N M1
N3 Lymph node(s) larger than 6 cm	
Pathological N (pN)	
NX Regional lymph nodes cannot be assessed	
pN0 No regional lymph node metastasis	
pN1 Metastasis in 4 or fewer lymph nodes	
pN2 Metastasis in more than 4 lymph nodes	
Distant Metastasis (M)	
M0 No distant metastasis	
M1 Distant metastasis	
Histologic Grade (G)	
No grading system exists for HPV-mediated oropharyngeal tumors	

Continued

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Staging selon TNM

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Table 5
American Joint Committee on Cancer (AJCC) TNM Staging System for the Larynx (8th ed., 2017)
(Non-epithelial tumors such as those of lymphoid tissue, soft tissue, bone or cartilage, and mucosal melanoma of the lip and oral cavity are not included)

Primary Tumor (T)	Glottis
TX Primary tumor cannot be assessed	T1 Tumor limited to the vocal cord(s) (may involve anterior or posterior commissure) with normal mobility
Tis Carcinoma in situ	T1a Tumor limited to one vocal cord
	T1b Tumor involves both vocal cords
Supraglottis	T2 Tumor extends to supraglottis and/or subglottis, and/or with impaired vocal cord mobility
T1 Tumor limited to one subsite of supraglottis with normal vocal cord mobility	T3 Tumor limited to the larynx with vocal cord fixation and/or invasion of paraglottic space and/or inner cortex of the thyroid cartilage
T2 Tumor invades mucosa of more than one adjacent subsite of supraglottis or glottis or region outside the supraglottis (eg, mucosa of base of tongue, vallecula, medial wall of pyriform sinus) without fixation of the larynx	T4 Moderately advanced or very advanced
T3 Tumor limited to larynx with vocal cord fixation and/or invades any of the following: postcricoid area, preepiglottic space, paraglottic space, and/or inner cortex of thyroid cartilage	T4a Moderately advanced or very advanced
T4 Moderately advanced or very advanced	T4b Very advanced local disease
T4a Moderately advanced local disease	Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures
Tumor invades through the outer cortex of the thyroid cartilage and/or invades tissues beyond the larynx (eg, trachea, soft tissues of neck including deep extrinsic muscle of the tongue, strap muscles, thyroid, or esophagus)	Subglottis
T4b Very advanced local disease	T1 Tumor limited to the subglottis
Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures	T2 Tumor extends to vocal cord(s) with normal or impaired mobility
	T3 Tumor limited to larynx with vocal cord fixation and/or inner cortex of the thyroid cartilage
	T4 Moderately advanced or very advanced
	T4a Moderately advanced local disease
	Tumor invades cricoid or thyroid cartilage and/or invades tissues beyond the larynx (eg, trachea, soft tissues of neck including deep extrinsic muscles of the tongue, strap muscles, thyroid, or esophagus)
	T4b Very advanced local disease
	Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures

Continued

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Approche thérapeutique – principes généraux

- En général une approche multidisciplinaire associant potentiellement:
 - Chirurgie
 - Radiothérapie
 - Chimiothérapie
- Idéalement une modalité unique dans les cas précoces
- Plusieurs buts de la prise en charge:
 - La guérison
 - La préservation de la fonction
 - Minimiser la toxicité surtout séquellaire

Discussion multidisciplinaire

- Idéalement, discussion de chaque cas dans le cadre d'une réunion multidisciplinaire impliquant:
 - Radiologues
 - Pathologues
 - Chirurgiens ORL et maxillo-faciaux
 - Radio-oncologues
 - Oncologues
 - Dentistes

Stratégie selon la localisation

- En général:
 - Nasopharynx: radio-chimiothérapie
 - Cavité buccale/cavité nasale/glandes salivaires:
 - Chirurgie +/- radio(chimio)thérapie adjuvante
 - Alternative pour la cavité buccale = curiethérapie, fréquente en FR mais rare en CH (compétences, culture)
 - Oro- et hypopharynx : RCT ou RT, parfois chirurgie (amygdale)
 - Larynx: chirurgie ou RT pour cas précoces, RCT pour cas avancés

La radiothérapie - stratégies

- Deux situations:
 - Exclusive
 - Adjuvante (post-opératoire), selon facteurs de risque pathologiques:
 - Tranches de section positives ou proches
 - Adénopathies multiples
 - Dépassement capsulaire ganglionnaire
 - Invasion lympho-vasculaire ou périnerveuse
 - Status HPV pour les tumeurs oropharyngés

La radiothérapie – considérations générales

- Une fois l'indication à la RT posée, plusieurs questions:
 - Locale (larynx) ou locorégionale (presque toujours)
 - Niveaux ganglionnaires à inclure?
 - Irradiation régionale bilatérale (en général) ou unilatérale (cas particuliers)
 - Avec ou sans chimiothérapie (ou cetuximab)
 - Fractionnement standard ou «altéré»
- Et plusieurs évaluations pré-RT
 - Besoin d'un soutien nutritionnel (selon perte de poids préalable, traitement prévu)
 - Evaluation du status dentaire et mesures prophylactiques

Le soutien nutritionnel

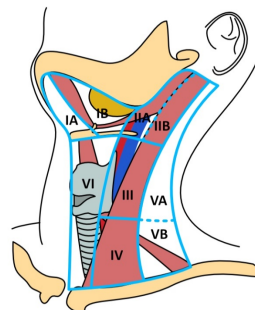
- Impliquer tôt un/e diététicien/ne ou nutritionniste
- Mesures allant du plus simple à des plus compliquées:
 - Conseils diététiques
 - Suppléments nutritifs oraux (SNO)
 - Sonde naso-gastrique (SNG)
 - Percutaneous endoscopic gastrostomy tube (PEG)
- Pas de consensus dans le débat SNG vs PEG, y compris en Suisse romande (HUG vs CHUV)

Bilan dentaire

- Une des complications les plus graves de la radiothérapie dans la sphère ORL et *l'ostéoradionécrose*
- Facteurs de risque:
 - Mauvaise hygiène buccale et état dentaire
 - Extractions ou infections futures
 - Xérostomie séquellaire à la RT
 - Moins bonne perfusion mandibulaire suite à la RT
 - Dose mandibulaire (Dmax = points chauds)
- Avec une bonne prévention (extractions prophylactiques, gouttières), risque très faible

Irradiation cervicale élective

- Niveaux à prendre de chaque côté du cou selon:
 - Localisation tumorale
 - Stade N (= atteinte ganglionnaire radiologique ou pathologique) +/- niveaux N+
 - En général, RT plus étendue du côté atteint, et moins étendue (ou pas du tout) du côté controlatéral



Level	Possible site of malignancy
IA	Lower lip, floor of mouth, lower gum
IB	Face, nose, paranasal sinuses, oral cavity, submandibular gland
II	Oral cavity, oropharynx, nasopharynx, hypopharynx, supraglottic larynx
III	Thyroid, larynx, hypopharynx, cervical esophagus
IV	Hypopharynx, larynx, thyroid, vertebral esophagus
V	Nasopharynx, thyroid, esophagus, lung, breast
VI	Lower lip, oral cavity, thyroid, glottic and subglottic larynx, apex of piriform sinus, cervical esophagus

Atlas de consensus pour les contours...

CT-based delineation of lymph node levels and related CTVs
in the node-negative neck: DAHANCA, EORTC, GORTEC, NCIC,
RTOG consensus guidelines

Vincent Grégoire^{a,*}, Peter Levendag^{b,1}, Kian K. Ang^c, Jacques Bernier^d, Marijel Braaksma^b,
Volker Budach^e, Cliff Chao^c, Emmanuel Coche^f, Jay S. Cooper^c, Guy Cosnard^f,
Avraham Eisbruch^c, Samy El-Sayed^g, Bahman Emami^c, Cai Grau^h, Marc Hamoirⁱ,
Nancy Lee^c, Philippe Maingon^l, Karin Muller^b, Hervé Reyhler^k

Irradiation unilatérale

- Pour certaines tumeurs de la cavité buccale ou de l'oropharynx (amygdale) bien latéralisées, avec une atteinte ganglionnaire limitée
- Tumeurs HPV+ de l'amygdale par exemple

L'intérêt de la chimiothérapie

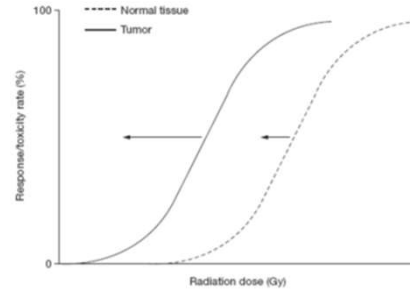
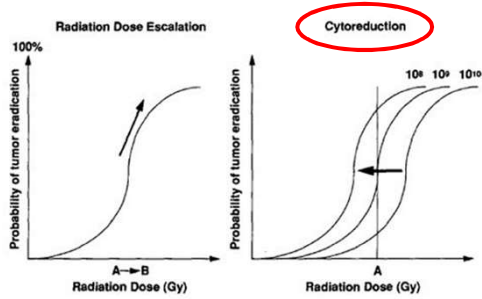
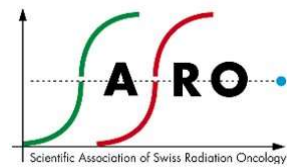
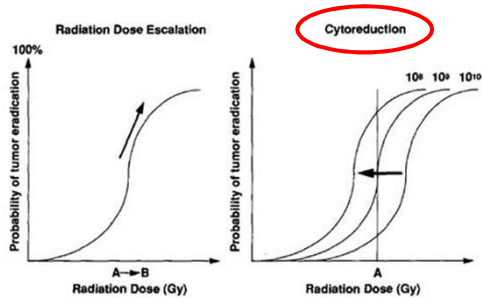
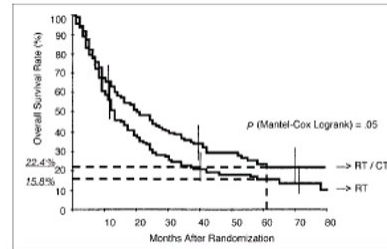
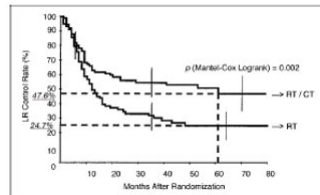


Figure 3 Schematic dose-response curves for tumor and normal tissue damage with radiation. The offset between the two curves indicates the therapeutic range. Chemoradiotherapy leads to a shift of both curves to the left, ideally with a stronger shift of the tumor curve (as indicated by the longer arrow), increasing overall efficacy of treatment (radiation enhancement).¹²³

L'intérêt de la chimiothérapie



La radio-chimiothérapie



La radio-chimiothérapie

- Méta-analyse MACH-NC
- > 100 études randomisées
- > 18'000 patients
- Conclusion: la chimiothérapie «concomitante» (cisplatine) augmente la survie globale à 5/10 ans d'environ 6,5/3,4%
- Seulement pour concomitante, pas en adjuvant ou induction



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HEAD AND NECK CANCER SYMPOSIUM

META-ANALYSES OF CHEMOTHERAPY IN HEAD AND NECK CANCER (MACH-NC): AN UPDATE

JEAN-PIERRE PINON, M.D., Ph.D.,* AURÉLIE LE MAÎTRE, M.Sc.,*
AND JEAN BOURRIS, M.D., Ph.D.,¹ ON BEHALF OF THE MACH-NC
COLLABORATIVE GROUP

*Biostatistics and Epidemiology Unit and ¹Department of Radiotherapy, Institut Gustave-Roussy, Villejuif, France

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COOPERATIVE GROUP

*Biostatistics and Epidemiology Unit and [†]Department of Radiotherapy, Institut Gustave-Roussy, Villejuif, France

La radio-chimiothérapie

- Aussi en post-opératoire...

Postoperative Irradiation with or without Concomitant Chemotherapy for Locally Advanced Head and Neck Cancer

Jacques Bernier, M.D., Ph.D., Christian Domenge, M.D., Mahmut Ozsahin, M.D., Ph.D., Katarzyna Matuszewska, M.D., Jean-Louis Lefebvre, M.D., Richard H. Greiner, M.D., Jordi Grali, M.D., Philippe Maingon, M.D., Frédéric Rolland, M.D., Michel Bolla, M.D., Francesco Cognetti, M.D., Jean Bourhis, M.D., Anne Kirkpatrick, M.Sc., and Martine van Glabbeke, M.Sc., for the European Organization for Research and Treatment of Cancer Trial 22931

La radio-chimiothérapie

- Aussi en post-opératoire...

Postoperative Irradiation with or without Concomitant Chemotherapy for Locally Advanced Head and Neck Cancer

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Toxicité de la RCT: négligée?

VOLUME 25 · NUMBER 26 · SEPTEMBER 10 2007

JOURNAL OF CLINICAL ONCOLOGY

REVIEW ARTICLE

Evaluation of Early and Late Toxicities in Chemoradiation Trials

Soren M. Bentzen and Andrea Trotti

From the University of Wisconsin

efficacy is unthinkable, it is unfortunately still true that many, if not most, trial reports fail to document toxicity in sufficient detail.⁹ Quan-

Toxicité: Bentzen

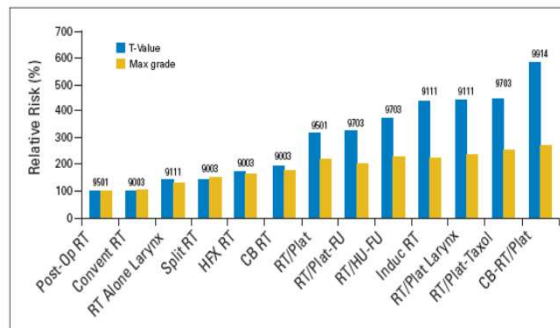


Fig 2. Toxicity burden measures: relative T-values versus relative maximum-grade values. Post-Op, postoperative; RT, radiotherapy; Convent, conventional; Plat, platinum; FU, fluorouracil; Induc, induction.

Le cetuximab (Erbix®)

- Anticorps anti-EGFR
- Étudié comme alternative au cisplatine, avec résultats initiaux prometteurs (tout aussi efficace mais moins toxique?)
- Finalement, pas moins toxique (plus?), et moins efficace
- En voie de disparition... (?)

THE NEW ENGLAND JOURNAL OF MEDICINE

ORIGINAL ARTICLE

Radiotherapy plus Cetuximab for Squamous-Cell Carcinoma of the Head and Neck

James A. Bonner, M.D., Paul M. Harari, M.D., Jordi Gialt, M.D., Nozar Azarnia, Ph.D., Dong M. Shin, M.D., Roger B. Cohen, M.D., Christopher U. Jones, M.D., Ranjan Sur, M.D., Ph.D., David Raben, M.D., Jacek Jassem, M.D., Ph.D., Roger Ove, M.D., Ph.D., Merrill S. Kies, M.D., Jose Baselga, M.D., Hagop Youssoufian, M.D., Nadia Amellal, M.D., Eric K. Rowinsky, M.D., and K. Kian Ang, M.D., Ph.D.*

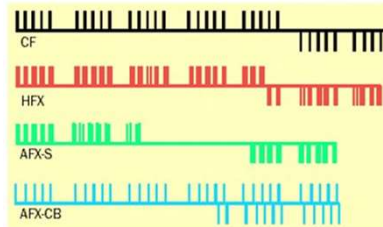
Fractionnement standard

- Classiquement (1,8 à) 2 Gy/fraction
- Dose tumorale = 70 Gy
- Dose élective = 50 Gy
- Niveaux de dose intermédiaires possibles pour zones cN+ ou pour les traitements adjuvants:
 - 66 Gy dans les zones de TS positive ou dépassement capsulaire
 - 60 Gy dans les zones de marges proches ou les niveaux ganglionnaires pN+
 - Etc...

Fractionnement «altéré»

- Fractionnement standard:
 - Une fraction/jour sur environ 7 semaines, à environ 2 Gy/fraction
- **Hyperfractionnement:**
 - Une dose totale plus élevée délivrée sur un même temps de traitement total, en plus de fractions (2 ou 3 par jour) avec une dose réduite par fraction
- **Fractionnement accéléré:**
 - La même dose et nombre de fractions délivrés sur un temps de traitement total moins long
- **Hypofractionnement ():**
 - Une dose totale moins élevée délivrée en moins de fractions sur moins de temps, avec une dose par fraction plus élevé

Fractionnement altéré



Fractionnement «accéléré»

- L'importance du temps total de traitement dans les cancers ORL (comme du col, canal anal, etc)
- Le «repopulation» accélérée, un des «5 R» de la radiobiologie
- A partir de la 4^e semaine de RT environ, un facteur de résistance
- D'où des stratégies pour accélérer la RT et diminuer le temps de traitement

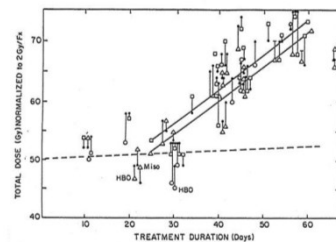
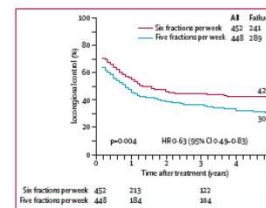
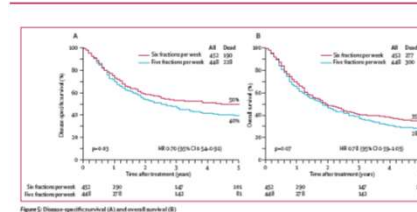


Fig. 1. TCD_{50} as a function of overall treatment time for squamous cell carcinomas of head and neck (Table 1). Data relate to T2 (○), T3 (□) or a combination of more than 2 stages (△). Total doses are normalized to the dose equivalent to that from a regimen of 2 Gy fractions using an α/β value of 25 Gy. Doses and times are best estimates of median values. The dose and control rate reported in the literature from which the TCD_{50} value was calculated is presented (●) to show the extent of the extrapolation. Rate of increase in TCD_{50} predicted from a 2 month clonogen doubling rate. (---). Estimated increase in TCD_{50} (—) with time for 'T3' (□) and mixed T stages (△) from independent scattergram analyses (Tables 2, 3) involving different data sets from those presented in this figure.

Fractionnement DAHANCA

- Deux séances le vendredi, séparées d'au moins 6 heures
- Raccourcit la durée totale de traitement d'une semaine, ce qui:
 - Augmente le contrôle loco-régional à 5 ans de 12%
 - Augmente la survie globale à 5 ans de 7%



Méta-analyse MARCH

Lancet Oncol. 2017 September ; 18(9): 1221–1237. doi:10.1016/S1470-2045(17)30458-8.

Role of radiotherapy fractionation in head and neck cancers (MARCH): an updated meta-analysis

Benjamin Lacas, MSc, Prof Jean Bourhis, MD, Prof Jens Overgaard, MD, Qiang Zhang, PhD, Prof Vincent Gregoire, MD, Matthew Nankivell, MSc, Prof Bjorn Zackrisson, MD, Zbigniew Szutkowski, MD, Prof Rafał Suwiński, MD, Prof Michael Poulsen, MD, Prof Brian O'Sullivan, MD, Prof Renzo Corvo, MD, Prof Sarbani Ghosh Laskar, MD, Prof Carlo Fallai, MD, Hideya Yamazaki, MD, Prof Werner Dobrowsky, MD, Kwan Ho Cho, MD, Prof Adam S Garden, MD, Prof Johannes A Langendijk, MD, Celia Maria Pais Viegas, MD, Prof John Hay, MBBChir, Prof Mohamed Lotayef, MD, Prof Mahesh K B Parmar, PhD, Anne Auperin, MD, Carla van Herpen, MD, Prof Philippe Maingon, MD, Prof Andy M Trotti, MD, Prof Cai Grau, MD, Jean-Pierre Pignon, MD, and Pierre Blanchard, MD, on behalf of the MARCH Collaborative Group†

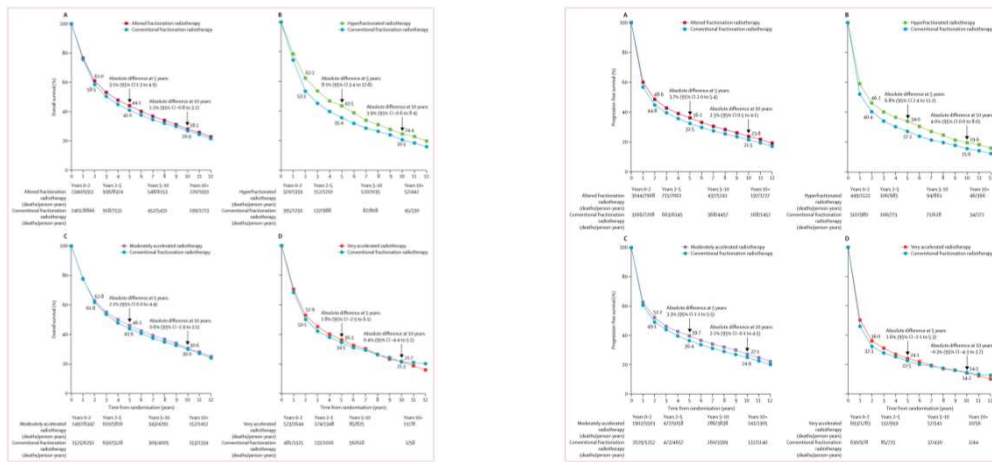
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Résultats MARCH



MARCH – conclusions

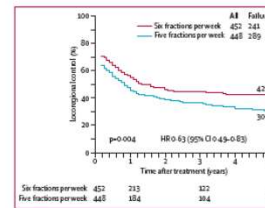
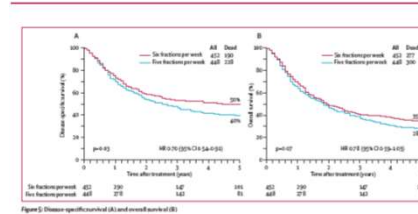
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- L'hyperfractionnement améliore les deux
- Alors...pourquoi est-ce que tous les patients ORL ne sont pas traités par hyperfractionnement?

MARCH – conclusions

- Le fractionnement accéléré améliore le contrôle loco-régional mais n'augmente pas de façon générale la survie globale
- L'hyperfractionnement améliore les deux
- Alors...pourquoi est-ce que tous les patients ORL ne sont pas traités par hyperfractionnement?
 - Problèmes logistiques
 - Pas de bénéfice en présence d'une chimiothérapie concomitante
 - Toxicité ++
 - --> en général, fractionnement(s) standard(s) en association avec la chimiothérapie

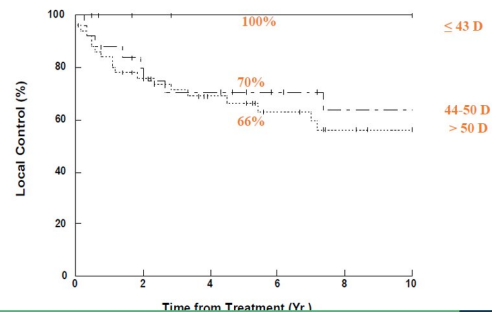
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Les cas des cancers précoces du larynx

- Meilleurs résultats surtout pour les tumeurs T2, mais aussi T1 avec 2,25 Gy/fraction
- Réduit le temps total de traitement...



Les cas des cancers précoces du larynx

Table 1. Patient allocation to Arm A and B

Arm	Tumor length <2/3 of glottis	Tumor length \geq 2/3 of glottis
Arm A (2 Gy/fr)		
A-1 (n = 31)	60 Gy/30 fr/6 wk	
A-2 (n = 57)		66 Gy/33 fr/6.6 wk
Arm B (2.25 Gy/fr)		
B-1 (n = 21)	56.25 Gy/25 fr/5 wk	
B-2 (n = 61)		63 Gy/28 fr/5.6 wk

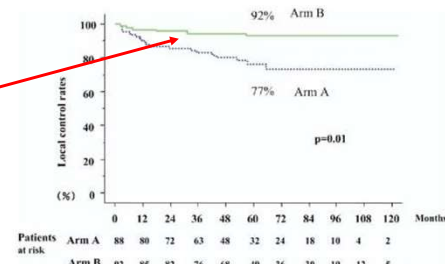
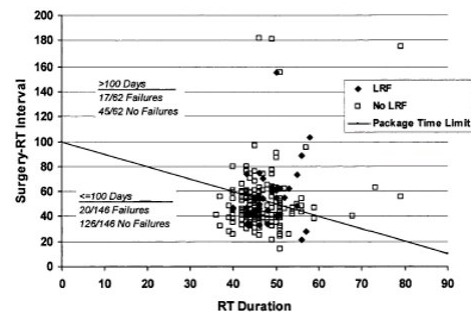


Fig. 1. Local control rates between Arms A and B.

Importance des délais aussi en adjuvant...

IMPORTANCE OF THE TREATMENT PACKAGE TIME IN SURGERY AND POSTOPERATIVE RADIATION THERAPY FOR SQUAMOUS CARCINOMA OF THE HEAD AND NECK

David I. Rosenthal, MD,¹ Li Liu, MD,¹ Jason H. Lee, MD,¹ Neha Vapiwala,²
Ara A. Chalian, MD,³ Gregory S. Weinstein, MD,³ Irina Chilian, MD,¹
Randal S. Weber, MD,³ Mitchell Machtay, MD¹



Qu'en est-il de l'hypofractionnement?

Practice Recommendations for Risk-Adapted Head and Neck Cancer Radiation Therapy During the COVID-19 Pandemic: An ASTRO-ESTRO Consensus Statement

Int J Radiation Oncol Biol Phys, Vol. ■, No. ■, pp. 1–10, 2020
0360-3016/\$ - see front matter © 2020 Elsevier Inc. All rights reserved.
<https://doi.org/10.1016/j.ijrobp.2020.04.016>

In scenario 2, risk mitigation with severely reduced radiation therapy capacity:

Use a hypofractionated radiation schedule.	Strong agreement
Reserve concomitant chemotherapy for use with conventional or mildly hypofractionated radiation therapy (≤ 2.4 Gy/f).	Agreement
Do not use induction chemotherapy to delay initiation of treatment.	Majority, near-agreement

Consensus sur le principe, pas les détails...

20 of 147 Automatic Zoom

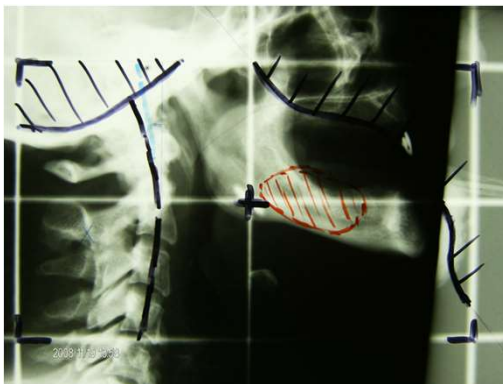
Hypofractionation Schedules in Late Pandemic Scenario for Oropharynx

Clinical case	Standard approach: percent agreement and favored schedules*	Scenario 1	Scenario 2
		Early pandemic: <i>risk mitigation</i> Change from standard: percent agreement and favored schedules*	Late pandemic: <i>severe shortage of radiation therapy capacity</i> Change from standard: percent agreement and favored schedules*
1. Oropharynx SCC T2N2bM0, p16 negative (OP-)	2.0-2.2 Gy/f (100%) (strong agreement) 70 Gy/35 f (63%) 70 Gy/33 f (17%) 65-66 Gy/30 f (13%)	No change (strong agreement)	Hypofractionated 2.41-3.0 Gy/f (70%) (strong agreement) 55 Gy/20 f (30%) 54 Gy/18 f (7%) 62.5-64 Gy/25 f (7%)

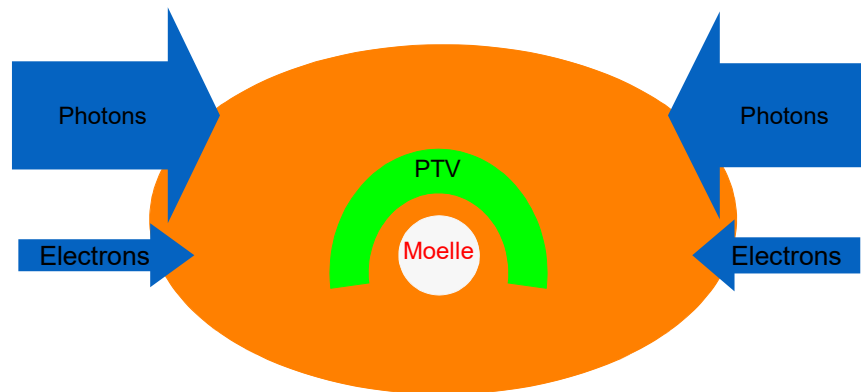
Hypofractionnement

- En résumé, à part pour les tumeurs précoces du larynx, pas de vraie place en ORL pour le moment
- (Il en est de même pour la SBRT (récidives?))
- Par contre, rappel (!):
 - Le fractionnement standard pour les irradiations mammaires est actuellement 40-42,5 Gy en 15 ou 16 fractions sur 3 semaines
 - Le fractionnement standard pour les irradiations prostatiques est actuellement 60-70 Gy en 20 à 28 fractions sur 4 à 5,5 semaines
 - Il n'existe plus aucun argument médical ou éthique pour faire autrement, malgré les comportements et pratiques assez désolants en Suisse romande...

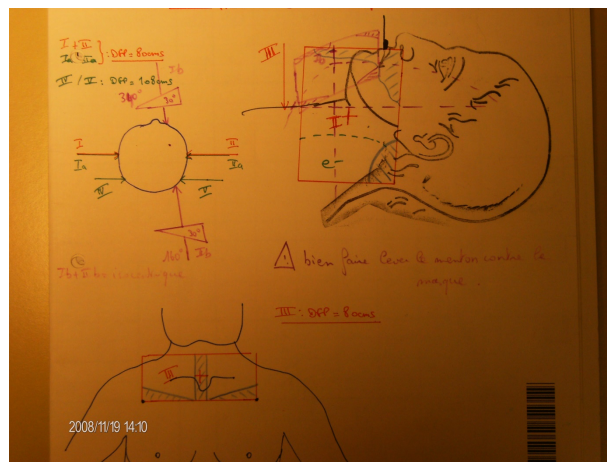
Il n'y a pas si longtemps...



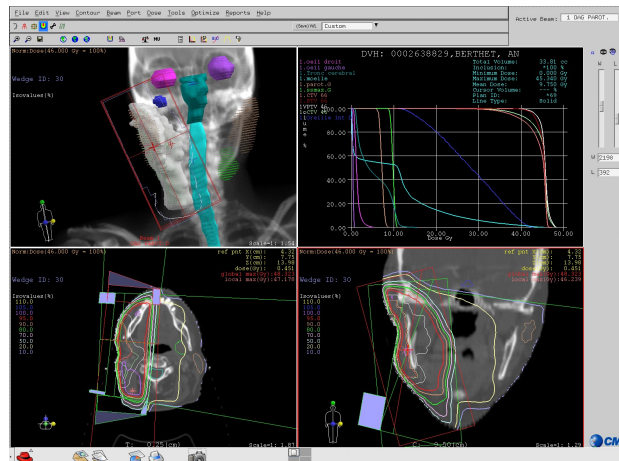
Planification 2D



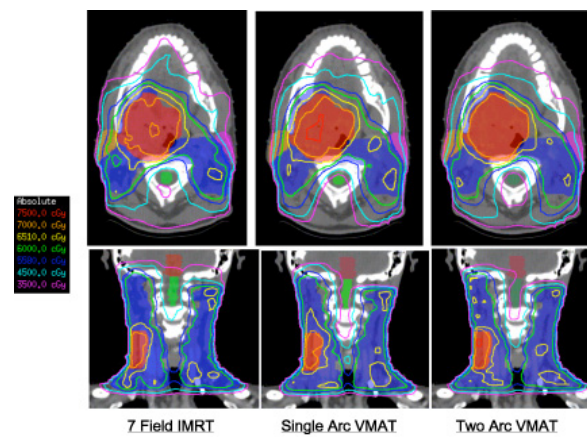
Plan de ttt circa 1990...



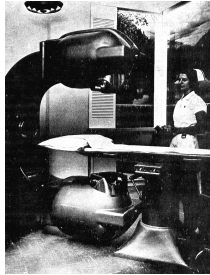
Circa 2000...



Aujourd'hui



Progrès techniques: machines/imagerie/informatique



kilovoltage

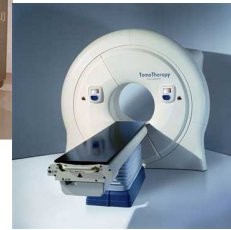


cobalt

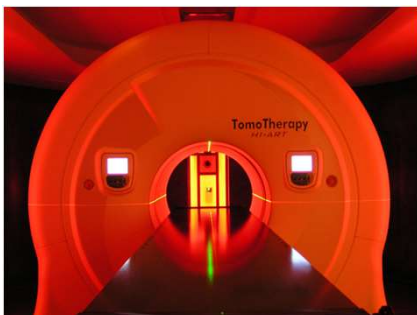
Linac (linear accelerator)



Tomotherapy®



Tomotherapy vs. Linac



Tomotherapy vs. Linac



Int. J. Radiation Oncology Biol. Phys., Vol. 65, No. 3, pp. 917-923, 2006
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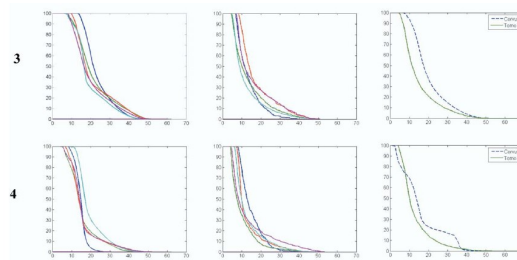
doi:10.1016/j.ijrobp.2006.02.038

PHYSICS CONTRIBUTION

INTENSITY-MODULATED RADIATION THERAPY (IMRT) DOSIMETRY OF THE HEAD AND NECK: A COMPARISON OF TREATMENT PLANS USING LINEAR ACCELERATOR-BASED IMRT AND HELICAL TOMOTHERAPY

KE SHENG, PH.D.,* JANELLE A. MOLLOY, PH.D.,[†] AND PAUL W. READ, PH.D., M.D.*

*Department of Radiation Oncology, University of Virginia, Charlottesville, VA; †Department of Radiation Oncology, Mayo Clinic, Rochester, MN



Fractionnement

- Classiquement en plusieurs phases avec boost(s) séquentiels (p.ex. 50 Gy + boost 20 Gy, le tout en 35 fractions)
- Avec l'IMRT/VMAT, nous sommes dans l'ère des SIB (boosts simultanés intégrés), avec pas mal de variations locales...
- En SIB, typiquement:
 - 70/66/59.4/54(52.8) Gy en 33 fractions de 2.12/2/1.8/1.64(1.6) Gy
 - 66/60/52.5 Gy en 30 fractions de 2.2/2/1.75 Gy
 - Etc...
 - Doses électives estimées comme biologiquement équivalentes aux doses classiques, en general env. 0.5 Gy/j de plus pour compenser temps plus long

Contours

- GTV si traitement exclusif, selon IRM/CT/PET-CT et examen clinique y compris description/dessins faits par l'ORL lors de son examen et la panendoscopie
- CTV tumoral
 - GTV + marges généreuses (1-1,5 cm en exclusif recommandé)
 - En adjuvant, lit tumoral/ADP + marges généreuses
- CTV électif
 - Niveaux ganglionnaires selon tumeur et stade
- PTV = en général CTV + 3-5 mm (masque et imagerie → peu de mouvement inter- ou intrafraction)

Immobilisation



VOLUME 24 · NUMBER 17 · JUNE 10 2006

JOURNAL OF CLINICAL ONCOLOGY

REVIEW ARTICLE

Intensity-Modulated Radiotherapy in the Standard Management of Head and Neck Cancer: Promises and Pitfalls

William M. Mendenhall, Robert J. Amdur, and Jatinder R. Palta

From the Department of Radiation Oncology, University of Florida College of Medicine, Gainesville, FL.

Submitted October 26, 2005; accepted February 22, 2006.

Authors' disclosures of potential conflicts of interest and author contributions are found at the end of this article.

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ABSTRACT

The purpose of this article is to review the role of intensity-modulated radiotherapy (IMRT) in the standard management of patients with head and neck cancer through a critical review of the pertinent literature. IMRT may result in a dose distribution that is more conformal than that achieved with three-dimensional conformal radiotherapy (3D CRT), allowing dose reduction to normal structures and thus decreasing toxicity and possibly enhancing locoregional control through dose escalation. Disadvantages associated with IMRT include increased risk of a marginal miss, decreased dose homogeneity, increased total body dose, and increased labor and expense. Outcomes data after IMRT are limited, and follow-up is relatively short. Locoregional control rates appear to be comparable to those achieved with 3D CRT and, depending on the location and extent of the tumor, late toxicity may be lower. Despite limited data on clinical outcomes, IMRT has been widely adopted as a standard technique in routine practice and clinical trials. The use of IMRT involves a learning curve for the practitioner and will continue to evolve, requiring continuing education and monitoring of outcomes from routine practice. Additional standards pertaining to a variety of issues, including target definitions and dose specification, need to be developed. Phase III trials will better define the role of IMRT in coming years.

Target delineation discrepancies

Strahlentherapie
und Onkologie

Original Article

The Reasons for Discrepancies in Target Volume Delineation

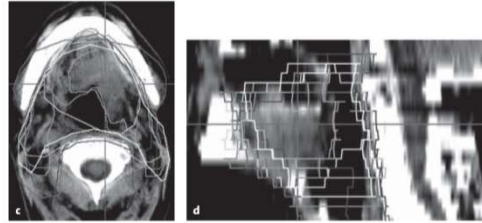
A SASRO Study on Head-and-Neck and Prostate Cancers

Wendy Jeanneret-Sozzi¹, Raphaël Moeckli², Jean-François Valley², Abderrahim Zouhair¹, Esat Mahmut Ozsahin¹, René-Olivier Mirimanoff¹ on Behalf of SASRO³

Purpose: To understand the reasons for differences in the delineation of target volumes between physicians.

Material and Methods: 18 Swiss radiooncology centers were invited to delineate volumes for one prostate and one head-and-neck case. In addition, a questionnaire was sent to evaluate the differences in the volume definition (GTV [gross tumor volume], CTV [clinical target volume], PTV [planning target volume]), the various estimated margins, and the nodes at risk. Coherence between drawn and stated margins by centers was calculated. The questionnaire also included a nonspecific series of questions regarding planning methods in each institution.

Jeanneret-Sozzi et al.



Figures 1a to 1d. Demonstration of the variations in the CTV delineation on axial and sagittal planes for the prostate (a, b) and the head-and-neck case (c, d).

Lymph node areas	Yes, homolateral	Yes, bilateral	No
Supraclavicular	0	8	2
Inferior jugular	0	7	2
Midjugular	1	9	0
Subdiaphragmatic	0	10	0
Superior jugular	0	10	0
Spinal	0	9	1
Submaxillary	0	9	1

Conclusion

In this study, we confirmed that wide interobserver variations exist in the delineation of GTV, CTV and PTV, in two different oncologic cases.

Data to explain these discrepancies are scarce in the literature and suggest multifactorial and complex reasons. We suggest that part of these are due to:

- (1) a variable knowledge and/or interpretation in the basic ICRU definitions;
- (2) difficulties in the identification of GTV due to the available imaging quality;
- (3) a variable understanding and/or concept for microscopic tumor extent (CTV);
- (4) a variable knowledge and/or concept in the estimation of variations in position and movement of the CTV (GTV);
- (5) a variable coherence between the theoretical knowledge (stated margins) and the practice (drawn margins).

Conceivably, measures can be taken to decrease discrepancies and, hopefully, improve interobserver coherence. To start with, a better and more comprehensive diffusion and understanding of ICRU recommendations in the radiation oncology community should be promoted. In parallel, continuous research in cancer imaging, in the knowledge of microscopic tumor extent and in a more systematic and individualized estimation of physiological motion should be supported.

Organes à risque

CT-based delineation of organs at risk in the head and neck region: DAHANCA, EORTC, GORTEC, HKNPCSG, NCIC CTG, NCRI, NRG Oncology and TROG consensus guidelines



Radiotherapy and Oncology, 2015-10-01, Volume 117, Issue 1, Pages 83-90.

Charlotte L. Brouwer, Roel J.H.M. Steenbakkers, Jean Bourhis, Wilfried Budach, Cai Grau, Vincent Grégoire, Marcel van

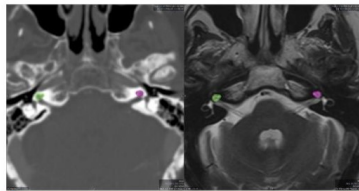


Fig. 2
Delineation of the cochlea in CT bone settings (left), matched to MRI-T2 (right).

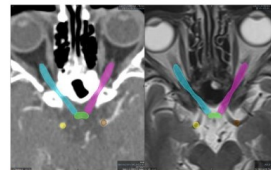
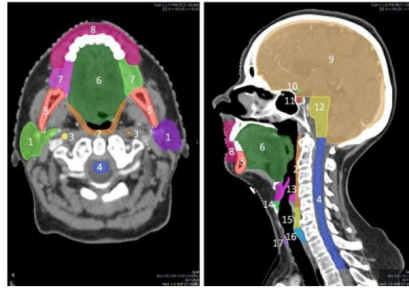
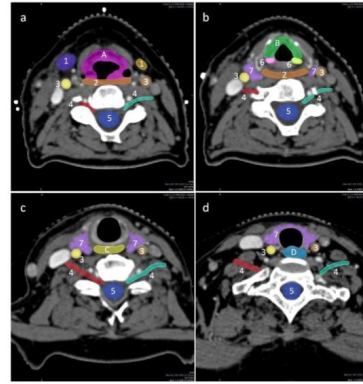


Fig. 3
Delineation of the optic nerves (blue and purple), optic chiasm (green) and carotid arteries (yellow and brown) on CT (left) and MRI-T2 (right).

De nombreuses structures à considérer...

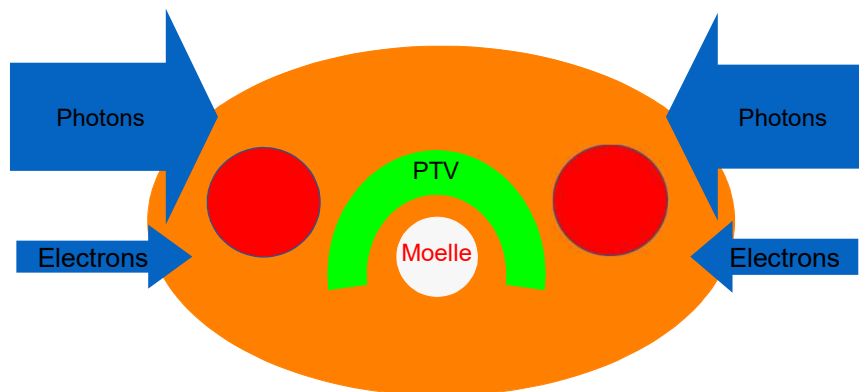


Axial (left) and sagittal (right) view of the consensus delineations of the parotid glands (1), pharyngeal constrictor muscles (2), carotid arteries (3), spinal cord (4), mandible (5), extended oral cavity (6), buccal mucosa (7), lips (8), brain (9), chiasm (10), pituitary gland (11), brainstem (12), supraglottic larynx (13), glottic area (14), crico-pharyngeal inlet (15), cervical esophagus (16) and thyroid (17). (For the full atlas, the reader is referred to the [Supplemental material](#).)

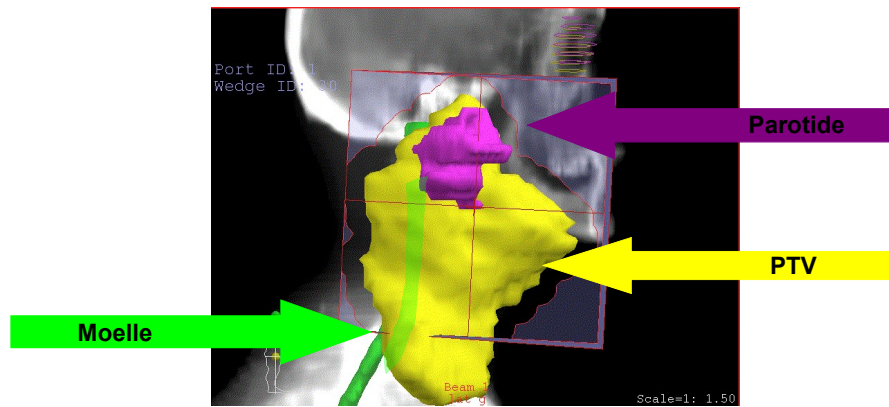


Axial CT slices showing the delineation of the supraglottic larynx (A) (a), glottic area (B) (b), crico-pharyngeal inlet muscle (C) (c), and cervical esophagus (D) (d). Other organs at risks visible are the submandibular glands (1), pharyngeal constrictor muscles (2), carotid arteries (3), brachial plexus (4), spinal cord (5), arytenoids (6) and thyroid

Les parotides



Les parotides



2D vs IMRT

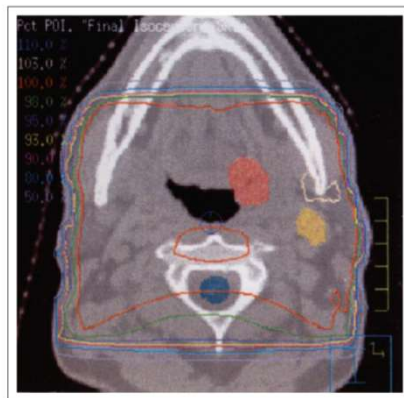


Fig 1. Axial dose distribution for a 49-year-old man with a T2N2C squamous cell carcinoma of the left tonsillar fossa. The patient received 76.8 Gy at 1.2 Gy per fraction twice daily with three-dimensional conformal radiotherapy followed by a

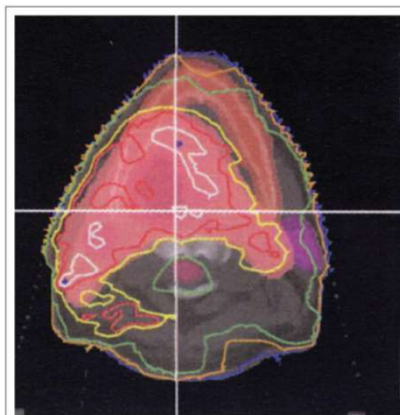
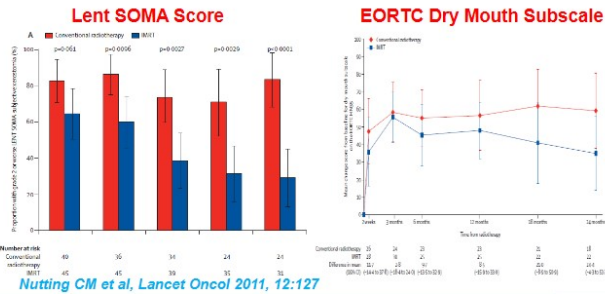


Fig 2. Axial dose distribution for a 56-year-old man with a T3N2B squamous cell

Etude PASSPORT

Parotid Sparing with IMRT Decreases Xerostomia: PASSPORT Trial

- 94 pts with OP/HP cancer randomized to IMRT vs 3DRT
- Whole contralateral parotid < 24Gy



A cautionary tale?



Int. J. Radiation Oncology Biol. Phys., Vol. 70, No. 3, pp. 660-665, 2008
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0360-3016/08/\$-see front matter

doi:10.1016/j.ijrobp.2007.09.018

RAPID COMMUNICATION

RECURRENCE IN REGION OF SPARED PAROTID GLAND AFTER DEFINITIVE INTENSITY-MODULATED RADIOTHERAPY FOR HEAD AND NECK CANCER

DONALD M. CANNON, B.S.,* AND NANCY Y. LEE, M.D.†

* Weill-Cornell Medical College, New York, NY; and † Department of Radiation Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY

Results: All patients had treatment failure in the region of a spared parotid gland. Failure in the 2 patients with bilateral multilevel nodal involvement occurred in the periparotid lymph nodes. The third patient developed a dermal metastasis near the tail of a spared parotid gland. On pretreatment imaging, the 2 patients with nodal failure had small nonspecific periparotid nodules that showed no hypermetabolic activity on positron emission tomography.

Conclusion: For HNC patients receiving definitive IMRT, nonspecific positron emission tomography-negative periparotid nodules on pretreatment imaging should raise the index of suspicion for subclinical disease in the presence of multilevel or Level II nodal metastases. Additional evaluation of such nodules might be indicated before sparing the ipsilateral parotid gland. © 2008 Elsevier Inc.

A cautionary tale



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doi:10.1016/j.ijrobp.2007.10.065

EDITORIAL

BEWARE THE SWING AND A MISS: BASEBALL PRECAUTIONS FOR CONFORMAL RADIOTHERAPY

PAUL M. HARARI, M.D.

University of Wisconsin School of Medicine and Public Health, Madison, WI

Despite the absence of Phase III trials rigorously comparing the long-term outcomes using highly conformal radiation techniques (intensity-modulated radiotherapy [IMRT], tomotherapy, proton therapy) vs. those using conventional techniques, there is a prevailing sentiment that improved dose conformality is “good” ... good for the patient, good for normal tissues and toxicity profiles, and good for the discipline of radiation oncology. The published data and evolving pat-

tion of new radiation delivery technologies in recent years. If radiation oncologists are reliably “hitting” all the tumor cells with radiation each day, and reliably sparing normal tissues, this improved conformality is indeed likely to be good (although questions remain unanswered regarding the long-range effect of radiation exposure to increased volumes of normal tissue). However, to use a baseball analogy, we would

Harari

Although idealized computer treatment plans with meticulous contours, sharp dose–volume histogram plots and steep isodose gradient profiles separating tumor from normal tissue are the norm in head-and-neck IMRT (particularly adjacent to the spinal cord and parotid glands), we know that the day-to-day variations in set up and delivery can degrade the integrity of idealized plans. It has been increasingly well appreciated

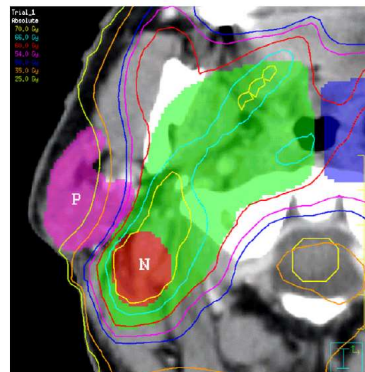


Fig. 1. Head-and-neck intensity-modulated radiotherapy plan illustrating steep dose gradient between metastatic superior jugular node (N) and right parotid gland (P). Tight juxtaposition between gross tumor (70 Gy prescription dose) and normal tissue avoidance structure (parotid gland, 26 Gy mean dose prescription) highlights potential risk that accompanies daily set-up and treatment variations during 30–35-fraction treatment course.

Harari

INADVERTENT OVEREMPHASIS ON SALIVA?

Parotid gland sparing in head-and-neck cancer treatment has emerged as a key objective for radiation oncologists in recent years. For decades previously, relatively little attention was paid to this issue because the available technology did not readily facilitate salivary gland sparing. For the most part, it was a given that patients would develop xerostomia after curative-intent radiotherapy for head and neck cancer. With our increasing capacity to spare salivary gland dose, the topic of xerostomia has taken center stage, with the desire to diminish toxicity and preserve better overall quality of life (3, 4). In the current era of highly conformal technology advancement, elegant normal tissue-sparing techniques sometimes attract as much, or more, attention as tumor eradication. For some patients with advanced head and neck cancer, this approach might not be warranted or safe despite the laudable desire to spare salivary gland function. Considerable

hensive radiation approaches. To paraphrase commentary from several head-and-neck cancer experts on this topic, "much better a dry mouth than a dead patient."

Parotid-sparing IMRT



ELSEVIER

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doi:10.1016/j.ijrobp.2006.09.021

CLINICAL INVESTIGATION

Head and Neck

THE IMPACT OF DOSE ON PAROTID SALIVARY RECOVERY IN HEAD AND NECK CANCER PATIENTS TREATED WITH RADIATION THERAPY

YUN LI, M.S.,* JEREMY M. G. TAYLOR, PH.D.,*[†] RANDALL K. TEN HAKEN, PH.D.,[†]
AND AVRAHAM EISBRUCH, M.D.[†]

*Department of Biostatistics, School of Public Health, University of Michigan, Ann Arbor, MI; [†]Department of Radiation Oncology, School of Medicine, University of Michigan, Ann Arbor, MI

Results: Parotids receiving higher radiation produce less saliva. The largest reduction is at 1–3 months after RT followed by gradual recovery. When mean doses are lower (e.g., <25 Gy), the model-predicted average stimulated saliva recovers to pretreatment levels at 12 months and exceeds it at 18 and 24 months. For higher doses (e.g., >30 Gy), the stimulated saliva does not return to original levels after 2 years. Without stimulation, at 24 months, the predicted saliva is 86% of pretreatment levels for 25 Gy and <31% for >40 Gy. We do not find evidence to support that the overproduction of stimulated saliva at 18 and 24 months after low dose in 1 parotid gland is the result of low saliva production from the other parotid gland.

Conclusions: Saliva production is affected significantly by radiation, but with doses <25–30 Gy, recovery is substantial and returns to pretreatment levels 2 years after RT. © 2007 Elsevier Inc.

IMRT and xerostomia

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JOURNAL OF CLINICAL ONCOLOGY

EDITORIAL

Reducing Xerostomia by IMRT: What May, and May Not, Be Achieved

Avraham Eisbruch, *Department of Radiation Oncology, University of Michigan, Ann Arbor, MI*

Kam et al⁸ found that in the patients treated with IMRT, significantly lower parotid gland mean doses were achieved compared with patients treated with 2D RT, and the lower doses translated into higher stimulated salivary flow rates. Moreover, the salivary flows in the IMRT patients improved over time, compared with no improvement in the 2D RT patients. These findings corroborate what we have known: following 2D RT of HN cancer, the salivary output is meager and does not improve over time. By

clear) by the part of the glands that received a low dose.** As the parotid salivary output is partially preserved and increasing over time, it has been predicted that parallel improvements in the symptoms of xerostomia would follow. However, this expected effect was found to be much more complex and uncertain. The uncer-

Altered Fractionation: Rappel

Fractionation for head and neck cancer

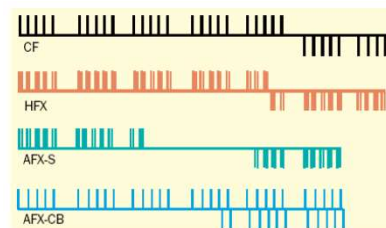
Review

Radiotherapy for cancer of the head and neck: altered fractionation regimens

Linh N Nguyen and K Kian Ang

The concept of accelerated repopulation describes that as tumours regress during the course of radiotherapy, the clonogenic surviving cells divide more rapidly, therefore reducing the overall effect of the fractionated radiotherapy.⁶ It was estimated that about 28 days after the start of radiotherapy, a dose increment of 0.6 Gy per day is required to compensate for repopulation in human head and neck cancers.

From these basic premises, two types of altered fractionation regimens were predicted to offer therapeutic advantage; accelerated fractionation regimens and hyperfractionation schedules.



Altered Fractionation

Hyperfractionated or accelerated radiotherapy in head and neck cancer: a meta-analysis



Jean Bourhis, Jens Overgaard, Hélène Audry, Kian K Ang, Michele Saunders, Jacques Bernier, Jean-Claude Horiot, Aurélie Le Maître, Thomas F Pajak, Michael G Poulsen, Brian O'Sullivan, Werner Dobrowsky, Andrzej Hliniak¹, Krzysztof Skladowski, John H Hay, Luiz H J Pinto, Carlo Fallai, Karen K Fu, Richard Sylvester, Jean-Pierre Pignon, on behalf of the Meta-Analysis of Radiotherapy in Carcinomas of Head and Neck (MARCH) Collaborative Group

Summary

Background Several trials have studied the role of unconventional fractionated radiotherapy in head and neck squamous cell carcinoma, but the effect of such treatment on survival is not clear. The aim of this meta-analysis was to assess whether this type of radiotherapy could improve survival.

Lancet 2006; 368: 843-54

See Comment page 819

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DOI:10.1016/S0140-

6736(06)69121-6

Radiation Oncology

Department (Prof J Bourhis MD)

and Biostatistics and

Epidemiology Department

14 Avenue de la République, F-69632, France

Your SIB, or mine?

Acta Oncologica
2008, 1-9, iFirst article

informa
healthcare

ORIGINAL ARTICLE

IMRT dose fractionation for head and neck cancer: Variation in current approaches will make standardisation difficult

KEAN F. HO¹, JACK F. FOWLER², ANDREW J. SYKES³, BENG K. YAP³, LIP W. LEE³ & NICK J. SLEVIN³

¹Academic Department of Radiation Oncology, University of Manchester, Manchester, UK, ²Emeritus, Department of Human Oncology and Medical Physics, University of Wisconsin, Wisconsin, USA and ³Department of Clinical Oncology, Christie Hospital NHS Foundation Trust, Manchester, UK

Dose fractionation radiotherapy trials in head and neck cancer over the past 20 years have established clinical benefits for a variety of modified fractionation schedules compared to the conventional 2 Gy per day to a total of 70 Gy over 7 weeks. When concurrent chemoradiation is used, there is further variation over the choice of optimum fractionation schedule. IMRT, with its potential for Simultaneous Integrated Boost (SIB), further adds to this uncertainty [1] such that there is an increasing lack of uniformity of practice with no single 'standard of care'.

In SIB, each target volume is treated to the same number of fractions and therefore receives a different dose per fraction. Planning studies suggest that this method produces the most conformal dose distribution compared with using sequential IMRT plans [2]. Although this offers the distinct advantage of

tailoring the appropriate dose to each target volume according to risk, it is a departure from the uniform fraction size conventionally employed.

There are now several published series of patients treated with head and neck IMRT which together demonstrate a plethora of fractionation regimens. It is apparent that single institutions are developing not only protocols that are 'in-house' but which are also evolving and changing with experience. We aim to examine the international practice of IMRT used for head and neck cancer through a survey of IMRT dose fractionation currently used in cancer centres around the world. A radiobiological comparison of the schedules is made. The variability of IMRT practice that currently exists is discussed with suggestions of possible reasons for this diversity in approach.

Phase III trials in RT?

VOLUME 26 · NUMBER 2 · JANUARY 10 2008

JOURNAL OF CLINICAL ONCOLOGY

COMMENTS AND CONTROVERSIES

Should Randomized Clinical Trials Be Required for Proton Radiotherapy?

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Cetuximab et RT: no toxicity?

Radiation Oncology



Short report

Open Access

Severe skin reaction secondary to concomitant radiotherapy plus cetuximab

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Figure 1
Exacerbated radiation dermatitis after cetuximab treatment.



Dysphagie et IMRT



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0958-3016/04/\$-see front matter

doi:10.1016/j.ijrobp.2004.05.050

CLINICAL INVESTIGATION

Head and Neck

DYSPHAGIA AND ASPIRATION AFTER CHEMORADIOTHERAPY FOR HEAD-AND-NECK CANCER: WHICH ANATOMIC STRUCTURES ARE AFFECTED AND CAN THEY BE SPARED BY IMRT?

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ROBIN MARSH, B.Sc.,* FRANK A. PAMEIJER, M.D.,[¶] AND ALFONS J. M. BALM, M.D.[‡]

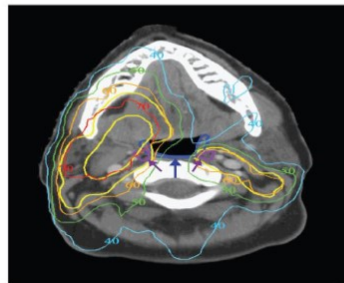
*Department of Radiation Oncology, University of Michigan, Ann Arbor, MI; Departments of [†]Radiation Oncology, [‡]Otolaryngology-Head and Neck Surgery, and [§]Radiology, and [¶]Section of Speech Therapy, The Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands

Réduire la dysphagie

Intensity-Modulated Chemoradiotherapy Aiming to Reduce Dysphagia in Patients With Oropharyngeal Cancer: Clinical and Functional Results

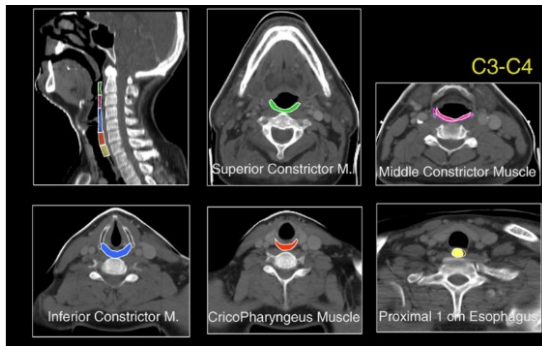
73 III/IV Opx 70Gy/7wks + taxol/carbo/wk

Med F/U 36mo 3yr LRC 96% DFS 88%



Feng JCO 2010

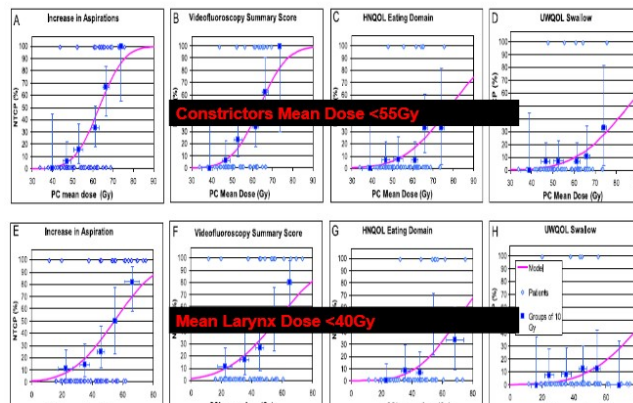
Muscles constricteurs pharyngés



Dysphagia-optimized IMRT/VMAT

IMRT reducing dysphagia complication probabilities • A. Eisbruch *et al.*

e97



Etude DARS

ICR The Institute of
Cancer Research

DARS

CANCER
RESEARCH
UK

The ROYAL MARSDEN
NHS Foundation Trust

First results of DARS: A Randomised Phase III Study of
Dysphagia-Optimised Intensity Modulated Radiotherapy (DO-
IMRT) versus Standard IMRT (S-IMRT) in Head and Neck
Cancer (CRUK/14/014)

Professor Christopher Nutting

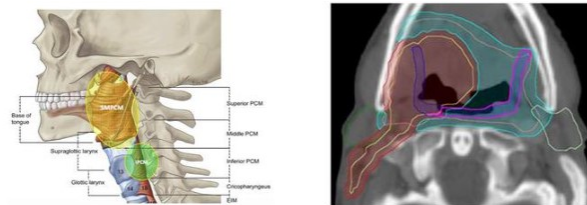
*C. Nutting, K. Rooney, B. Foran, L. Pettit, M. Beasley, L. Finneran, J. Roe, J. Tyler,
T. Roques, A. Cook, I. Petkar, S. Bhide, D. Srinivasan, C. Boon, E. De Winton, R. Frogley,
K. Mertens, M. Emson, E. Hall on behalf of the DARS Investigators*

ASCO 2020

DARS

Dysphagia-Optimised IMRT

4



- The volume of the superior & middle pharyngeal constrictor muscle (PCM) or inferior PCM **lying outside the high-dose clinical target volume (CTV65)** was set a mandatory mean dose constraint (<50 Gy) in DO-IMRT

DARS

UW-QOL swallowing at 12 months

18

Q5 Swallowing question of UW-QOL

	S-IMRT N (%)	DO-IMRT N (%)	
I can swallow as well as ever	7 (15.2)	21 (40.4)	+25%
I cannot swallow certain solid foods	37 (80.4)	30 (57.7)	-23%
I can only swallow liquid food	1 (2.17)	1 (1.92)	
I cannot swallow because it "goes down the wrong way" and chokes me	1 (2.17)	0	

Quand l'IMRT ne suffit pas....

- Paul Scherrer Institute, Villigen



Some proton / IMXT comparisons - 4. maxillary sinus MGH

3 Target Volumes

Gross volume: 76Gy
 Subclinical: 66Gy
 Microscopic: 54Gy

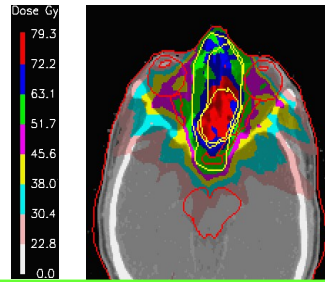
Nominal constraints

Optic nerves < 56Gy
 Brainstem < 53Gy
 Eyes < 50Gy

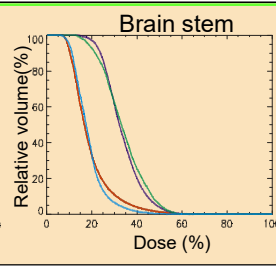
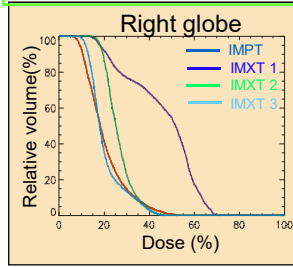
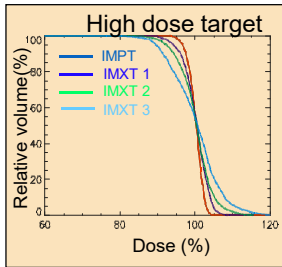
Nominal IMPT



Nominal IMXT



Loss of dose homogeneity and conformity to target volumes



L'immunothérapie dans les cancers ORL?

Radiation and checkpoint blockade immunotherapy: radiosensitisation and potential mechanisms of synergy

Andrew B Sharabi, Michael Lim, Theodore L DeWeese, Charles G Drake *Lancet Oncology* 2015; 16: e498-509

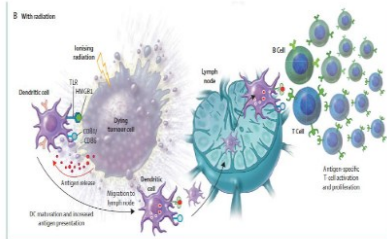


Figure 2: Radiation enhances cross-presentation of tumour antigens. (A) In the absence of danger signal, tumour antigen presentation is restricted or tolerogenic. (B) Radiation-induced danger signals enhance dendritic cell-mediated antigen presentation, resulting in activation and proliferation of tumour-specific CD8 T cells, TCR-T cell receptor.

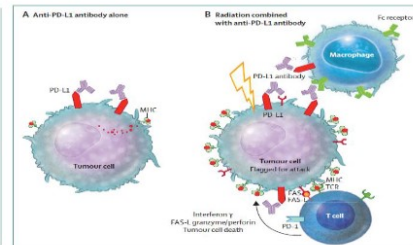
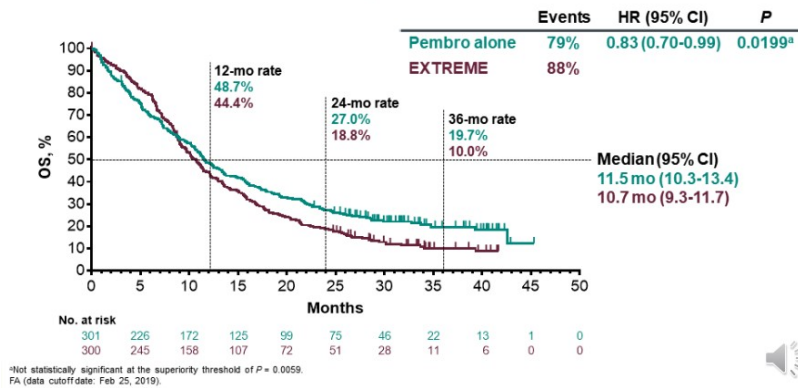


Figure 3: Radiation combined with checkpoint blockade immunotherapy increases tumour cell susceptibility to immune-mediated cell death. (A) Anti-PD-L1 alone is most pro-tolerantly effective. (B) Radiation combined with anti-PD-L1 upregulates MHC and FAS-L on tumour cells, increasing susceptibility to T-cell mediated cytotoxicity. TCR-T cell receptor.

KEYNOTE-048 pour patients M1

OS, P vs E, Total Population

Rischin KN048 ASCO 2019

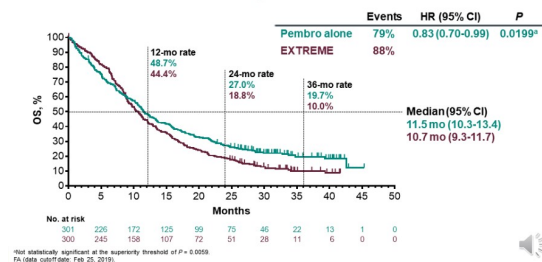


Etude KEYNOTE-048

- A établi l'immunothérapie par pembrolizumab (Keytruda®) seul comme nouveau standard en 1^{ère} ligne métastatique

OS, P vs E, Total Population

Rischin KN048 ASCO 2019



Etude JAVELIN 100 et autres

- Données négatives, aucun bénéfice de l'association immunothérapie et RT en situation curative
- La chimiothérapie concomitante de cisplatine reste le standard

Radiation and checkpoint blockade immunotherapy: radiosensitisation and potential mechanisms of synergy

Andrew B. Sharabi, Michael Ling, Theodore I. DrWess, Charles G. Drake
Lancet Oncology 2015; 16: 938-949

