



Associazione Italiana  
**Radioterapia Oncologica**  
Gruppo Interregionale  
Lazio/Abruzzo/Molise

## Le terapie di supporto in Radioterapia: **Verso una Guida Pratica**

Lunedì 4 Dicembre 2017  
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### Tossicità nei trattamenti del distretto Testa-Collo

# Xerostomia

## Cenni di patogenesi e Strumenti di valutazione

V De Sanctis



# XEROSTOMIA

**Anormale secchezza della bocca dovuta a  
insufficiente secrezione/produzione di saliva**



# La Saliva gioca un ruolo vitale nel mantenere la corretta igiene e appropriato funzionamento del cavo orale

**Acqua 99%** del volume salivare.

il rimanente **1%**

## **Sali inorganici**

sodium

potassium

calcium

magnesium

## **Composti organici**

colesterolo

Acido urico

proteine (lattoferrina, lactoperossidasi, lisozima,amilasi, maltasi)

# Principali funzioni della saliva

**Preparazione del bolo alimentare**

**Modulazione del gusto**

**Iniziale digestione del bolo tramite le amilasi e maltasi**

**Mantenimento del pH orale tra 6.8–7.2**

**Mantenimento dell'integrità della mucosa orale**

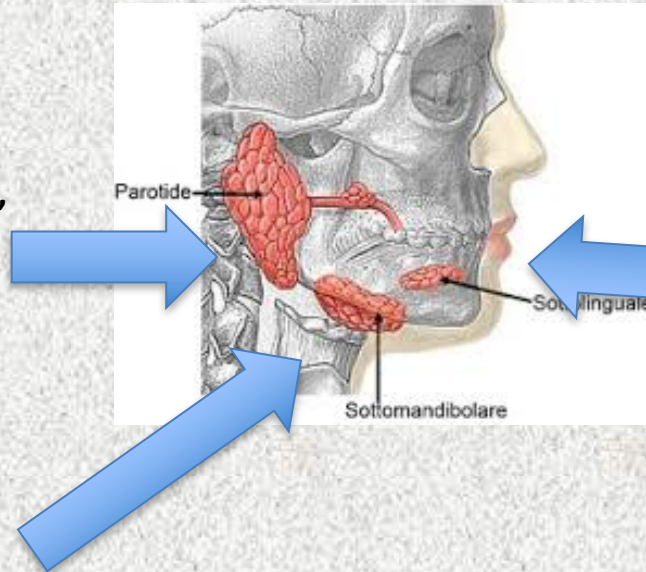
**Effetto antibatterico per la presenza di lattoferrina e lisozima**

,



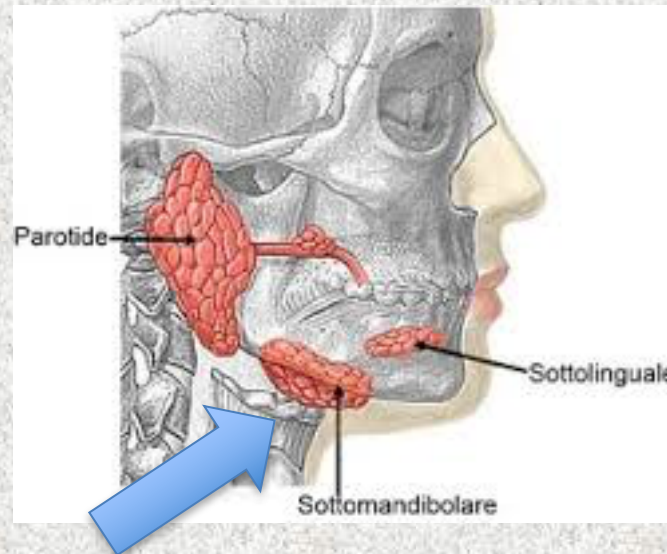
**Le ghiandole salivari maggiori  
(parotide, sottomandibolari e sublinguali)  
Producono più del 90% delle secrezioni salivari,  
con una produzione media giornaliera  
di 1000 - 1500 mL.**

La ghiandola parotide produce un fluido acquoso e ricco di proteine, **50% della secrezione stimolata**



Le ghiandole salivari minori producono 10% dell'intero volume salivare, ma hanno un ruolo importante nella **lubrificazione continua della mucosa**

Le ghiandole sottomandibolari hanno una **secrezione continua** di saliva sierosa e mucoide **>60% della secrezione giornaliera non stimolata**



È responsabile della maggior parte della secrezione della saliva a riposo **durante le ore del sonno**, mantenendo una normale lubrificazione della mucosa

### Xerostomia: A day and night difference

Tim Dijkema<sup>a,\*</sup>, Cornelis P.J. Raaijmakers<sup>a</sup>, Pètra M. Braam<sup>a,1</sup>, Judith M. Roesink<sup>a</sup>, Evelyn M. Monninkhof<sup>b</sup>, Chris H.J. Terhaard<sup>a</sup>

Radiotherapy and Oncology 104 (2012) 219–223

*Conclusions:* Differentiating between complaints during day- and nighttime in xerostomia research is necessary. Dry mouth at night is a frequent problem after (parotid-sparing) RT for HNC and is explained by submandibular gland dysfunction. Sparing of the contralateral submandibular gland, in addition to parotid gland sparing, may result in improved patient-reported xerostomia.

## **La salivazione puo' essere ridotta**

**Anziani (29% to 77%)**

**e associata a varie patologie**

**Artrite reumatoide**

**Sjogren's syndrome**

**HIV**

**diabete**

**Ipertensione**

# Xerostomia e farmaci

**Table 2.** Select drug types that may cause or exacerbate xerostomia.<sup>4,15</sup>



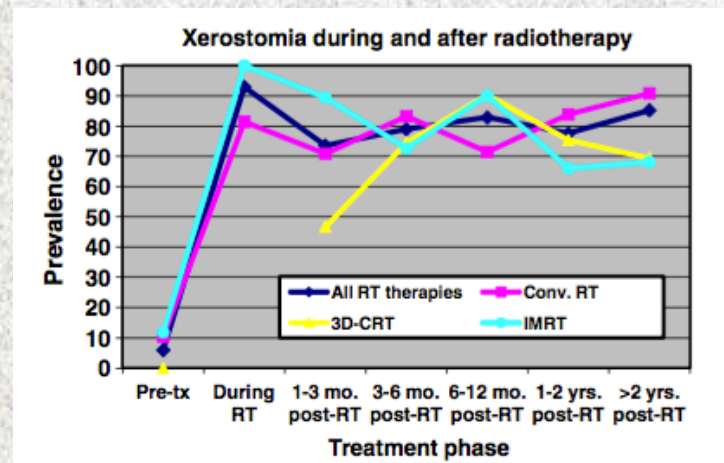
Anorexiant  
Antiacne agents  
Antianxiety agents  
Anticholinergic/antispasmodic agents  
Anticonvulsants  
Antidepressants  
Antidiarrheal agents  
Antihistamines  
Antihypertensive agents  
Anti-inflammatory analgesic agents  
Antiemetic agents  
Antiparkinsonian agents  
Antipsychotic agents  
Bronchodilators  
Chemotherapy agents  
Decongestants  
Diuretics  
Muscle relaxants  
Narcotic analgesics  
Sedatives



**Virtualmente tutti i pazienti sottoposti a radioterapia per tumori del testa collo mostrano un qualche grado di xerostomia come risultato del danno da radiazioni delle ghiandole salivari**

**Alcuni studi hanno riportato una riduzione del flusso salivare del 90% a tre mesi con la 3DCRT e del 20-40% con IMRT**

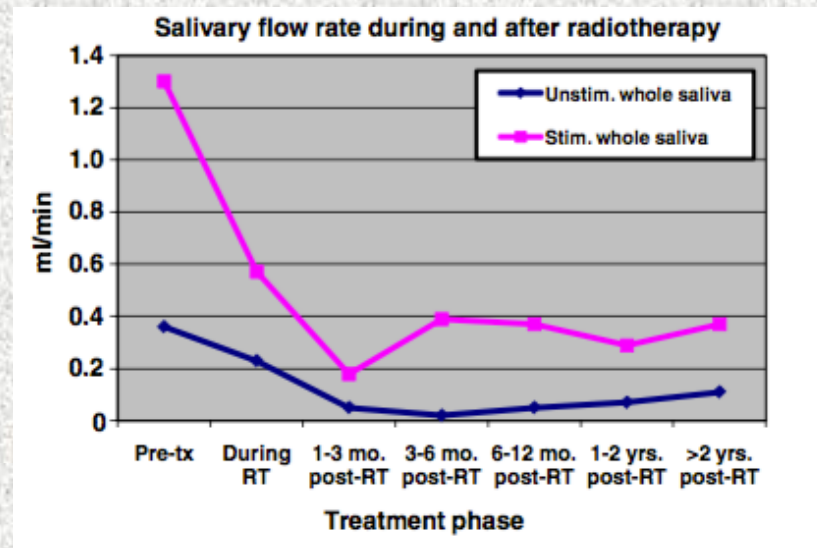
Nutting, Lancet Oncol 2011;12:127–36.



**Virtualmente tutti i pazienti sottoposti a radioterapia per tumori del testa collo mostrano un qualche grado di xerostomia come risultato del danno da radiazioni delle ghiandole salivari**

**Il flusso salivare può anche recuperare dopo la radioterapia, con un incremento di circa il 32% dopo 1-5 anni dal trattamento radioterapico**

Braam 2005



## **quantità**

**un decremento del flusso salivare del 50-60% durante la 1 settimana, che si riduce al 20 % rispetto al basale alla 7° settimana di trattamento**

## **qualità**

**dopo radioterapia un decremento dell'attività delle amilasi, dei bicarbonati e del pH e un significativo incremento della osmolarità, viscosità, lattoferrina, proteine, calcio e alterazione della composizione delle mucine.**

**Sebbene il danno da radiazioni alle ghiandole salivari è un fenomeno noto l'esatto meccanismo non è stato ancora ben definito**

**Nel 1911 Jean Bergonie ha descritto la radiosensibilità delle ghiandole salivari un **enigma**.**

**Le cellule funzionali (escretorie, acinari) sono altamente differenziate e hanno un basso turn-over cellulare, ma si comportano come cellule indifferenziate**

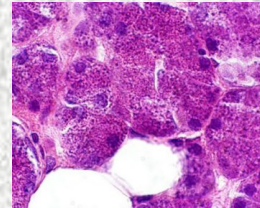
**Classicamente**

**tessuti con basso "mitotic rate" non dovrebbero essere particolarmente radiosensibili**

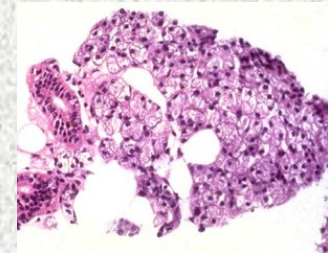


**Danno da radiazioni delle  
ghiandole salivari**  
**Meccanismo a due steps**

**Fase precoce**



**Danno funzionale**



**Deficit delle funzioni cellulari**

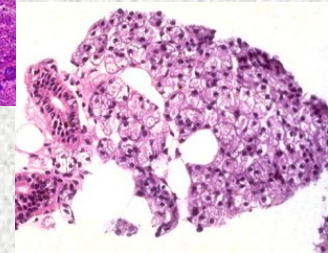
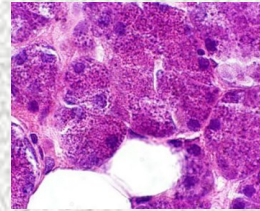
**a causa**

**di un danno selettivo della membrana cellulare  
che interferisce sul sistema recettore-mediato del  
meccanismo di escrezione dell'acqua**

**Danno da radiazioni delle  
ghiandole salivari**  
**Meccanismo a due steps**

**Fase precoce**

**Danno funzionale**



**Escrezione dell'acqua è ridotta già del 60% rispetto alle condizioni basali entro 3 giorni dall'inizio della radioterapia, mentre la secrezione di amilasi rimane nella norma**

**No morte cellulare o lisi cellulare in queste fasi precoci**

# Danno da radiazioni delle ghiandole salivari

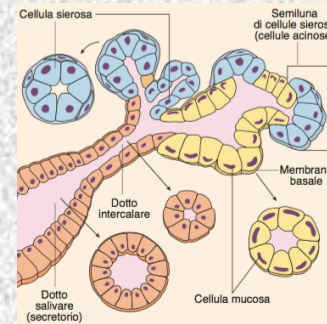
## Meccanismo a due steps

### fase tardiva

Classico “cell killing”  
delle cellule progenitrici e delle “stem  
cells”

1) Inibizione di un' appropriata  
ripopolazione

2) Danno al microambiente



# Xerostomia come un danno tardivo

## killing delle "stem cells"

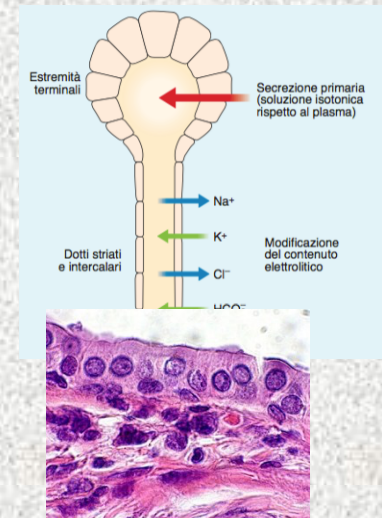
### danno tardivo



Alterato  
funzionamento delle  
cellule secretorie  
dovuto a progenitor  
cell death



Nuove cellule acinari  
non funzionano  
correttamente a  
causa  
danno ai dotti e al  
microcircolo



**Saliva si modifica**

Da una secrezione liquida con pH neutro  
A una secrezione vischiosa a incrementata  
acidità

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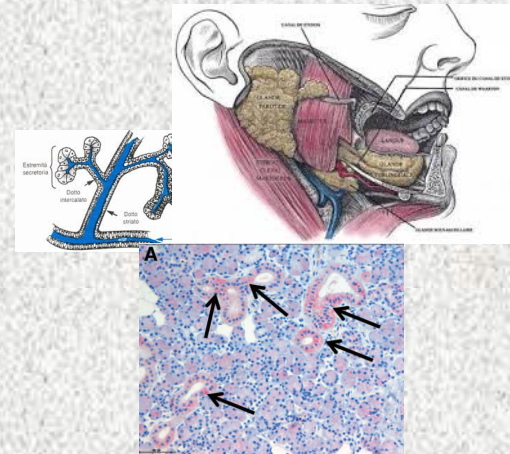
# Understanding mechanisms yields novel approaches to reduce radiotherapy-related xerostomia

Peter van Luijk, Johannes Albertus Langendijk, Robert Paul Coppes

February 2017

**Le cellule staminali sono state identificate come responsabili della rigenerazione cellulare nelle ghiandole salivari dopo radioterapia**

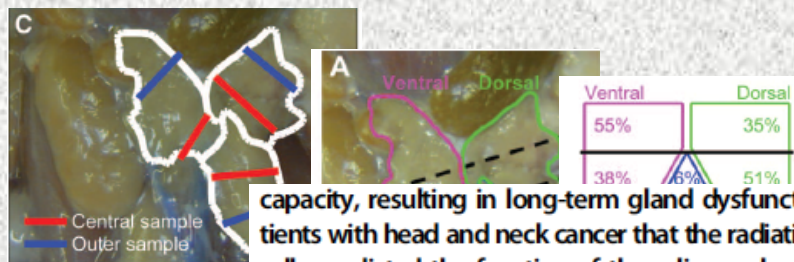
**Sono soprattutto localizzate a livello dei dotti principali delle ghiandole**



**Sparing the region of the salivary gland containing stem cells preserves saliva production after radiotherapy for head and neck cancer**

Peter van Luijk,<sup>1\*</sup> Sarah Pringle,<sup>1,2</sup> Joseph O. Deasy,<sup>3</sup> Vitali V. Moiseenko,<sup>4</sup> Hette Faber,<sup>1,2</sup>

ScienceTranslationalMedicine.org 16 September 2015



capacity, resulting in long-term gland dysfunction with reduced saliva production. Then we showed in a cohort of patients with head and neck cancer that the radiation dose to the region of the salivary gland containing the stem/progenitor cells predicted the function of the salivary glands one year after radiotherapy. Finally, we showed that this region of the salivary gland could be spared during radiotherapy, thus reducing the risk of post-radiotherapy xerostomia.

Phase III randomised trial

## Novel approaches to improve the therapeutic index of head and neck radiotherapy: An analysis of data from the PARSPORT randomised phase III trial

Florian Buettner<sup>a,\*</sup>, Aisha B. Miah<sup>b</sup>, Sarah L. Gulliford<sup>a</sup>, Emma Hall<sup>c</sup>, Kevin J. Harrington<sup>b</sup>, Steve Webb<sup>a</sup>,  
Mike Partridge<sup>a</sup>, Christopher M. Nutting<sup>b</sup>

Radiotherapy and Oncology 103 (2012) 82–87

**Table 4**  
Area under the curve for different grading schemes.

	Morphological model	Mean whole	Mean contra	Mean sup. comb.	Mean contra $\geq 26$ Gy
<i>(a) LENT/SOMA</i>					
Nasopharynx	0.80	0.50	0.56	0.50	0.53
PARSPORT II	0.69	0.54	0.39	0.54	0.66
<i>(b) RTOG</i>					
PARSPORT	0.77	0.63	0.68	0.64	0.64
Nasopharynx	0.81	0.57	0.59	0.57	0.49
PARSPORT II	0.96	0.36	0.19	0.48	0.65

**Results:** The predictive accuracy of dose–response models improved significantly when including regional variations of radiosensitivity of the parotid glands compared to standard mean-dose models ( $p = 0.001$ ,  $t$ -test). Beneficial dose-pattern analysis demonstrated the importance of minimising dose to the lateral and cranial component of the human parotid gland in order to avoid xerostomia. Furthermore we found an evidence that surgical removal of the sub-mandibular gland significantly increases the risk of radiation-induced xerostomia.

**Conclusion:** Dose–response models which take the shape of the dose-distribution into account predicted xerostomia significantly better than standard mean-dose models. Our novel model could be used to rank potential treatment plans more reliably according to their therapeutic index and may be useful to generate better treatment plans.

**Parotid-gland Stem-cell Sparing Intensity-modulated radiotherapy  
prospective double-blind randomized controlled trial comparing parotid  
sparing IMRT to stem cell sparing IMRT**

**(<https://clinicaltrials.gov/ct2/show/NCT01955239>).**

**Combining both arms of the trial will yield data in which the correlation between dose to the whole gland and dose to its stem cell region is reduced, providing better insight in the question which dose metric is most critical for the response of the gland.**

**University Medical Center Groningen  
ClinicalTrials.gov Identifier:  
NCT01955239  
First Posted: October 7, 2013  
Last Update Posted: June 22, 2017**

**Pringle S, Van Os R, Coppes RP.**

**Concise review: Adult salivary gland stem cells and a potential therapy for xerostomia.**

**Stem Cells. 2013 Apr;31(4):613-9.**

**Pringle S, Maimets M, van der Zwaag M, et al.**

**Human Salivary Gland Stem Cells Functionally Restore Radiation Damaged Salivary Glands.**

**Stem Cells 2016;34:640-52**

**Jensen DH, Oliveri RS, Trojahn Kølle SF,**

**Mesenchymal stem cell therapy for salivary gland dysfunction and xerostomia: a systematic review of preclinical studies.**

**Oral Surg Oral Med Oral Pathol Oral Radiol. 2014 Mar;117(3):335-342.**



**The QUANTEC criteria for parotid gland dose and their efficacy to prevent moderate to severe patient-rated xerostomia**

IVO BEETZ

Acta Oncologica, 2014; 53: 597–604

**“QUANTEC Group concluded that severe xerostomia, defined as long-term stimulated salivary flow 25% of baseline, can be reduced if at least one parotid gland is spared with a mean dose of less than 20 Gy or if both glands are spared with a mean dose of less than 25 Gy” .**

**“When the QUANTEC criteria were met, the rate of grade 4 xerostomia, defined as 25% reduction of pretreatment salivary flow measured at 3 months was 40% but indeed improved to less than 20% at 12 months”.**

Recupero del flusso salivare e il grado di xerostomia post-IMRT è migliore nei pazienti in cui la ghiandola **sottomandibolare controlaterale** è stata risparmiata

Distribuzione di dose alle **ghiandole salivari minori** è ancora **oggetto di discussione**

**CONTRO** limitato significato riguardo alla disfunzione salivare sulla base di scale patient-rated symptoms

**PRO** la dose di radiazione alla cavità orale ,come surrogato per la dose alle ghiandole minori , è predittiva della severità della xerostomia

# NTCP models for patient-rated xerostomia and sticky saliva after treatment with intensity modulated radiotherapy for head and neck cancer: The role of dosimetric and clinical factors <sup>☆</sup>

Ivo Beetz <sup>a,\*</sup>, Cornelis Schilstra <sup>a</sup>, Arjen van der Schaaf <sup>a</sup>, Edwin R. van den Heuvel <sup>b</sup>, Patricia Doornaert <sup>c</sup>,

Radiotherapy and Oncology 105 (2012) 101–106

**Purpose:** The purpose of this multicentre prospective study was to develop multivariable logistic regression models to make valid predictions about the risk of moderate-to-severe patient-rated xerostomia (XER<sub>M6</sub>) and sticky saliva 6 months (STIC<sub>M6</sub>) after primary treatment with intensity modulated radiotherapy (IMRT) with or without chemotherapy for head and neck cancer (HNC).

Logistic regression coefficients and odds ratios for the NTCP models for patient-rated xerostomia and for patient-rated sticky saliva 6 months after treatment. The constant refers to the constant of the logistic regression formula.

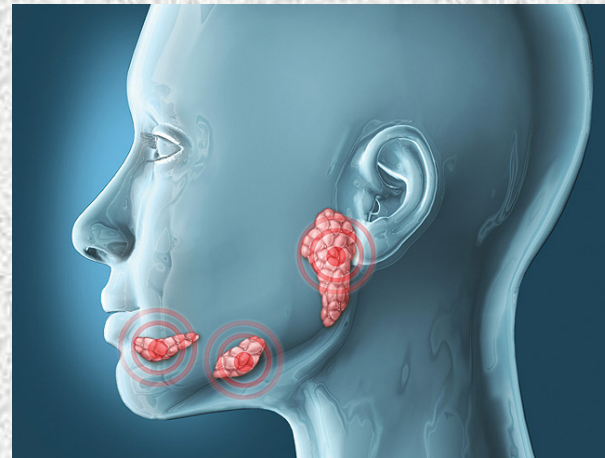
NTCP model	Variable	$\beta$	p-value	Odds ratio	95% CI
Patient-rated xerostomia	Mean dose contralateral parotid gland (Gy)	0.047	<0.01	1.05	1.02–1.08
	Baseline xerostomia score (none vs. a bit)	0.720	0.05	2.05	1.00–4.23
	Constant	–1.443	<0.01		
Patient-rated sticky saliva	Mean dose contralateral submandibular gland (Gy)	0.075	<0.01	1.08	1.03–1.13
	Mean dose sublingual glands (Gy)	–0.060	0.01	0.94	0.90–0.98
	Mean dose soft palate (Gy)	0.026	0.04	1.03	1.00–1.05
	Constant	–3.243	<0.01		

**Conclusions:** The multivariable NTCP models presented in this paper can be used to predict patient-rated xerostomia and sticky saliva. The dose volume parameters included in the models can be used to further optimise IMRT treatment.

# XEROSTOMIA

**Anormale secchezza della bocca dovuta a  
insufficiente secrezione/produzione di saliva**

**Diagnostic  
workout**





## **Scialometria**

**Sebbene la scialometria può direttamente misurare la funzione escrettrice della ghiandola salivare, ha alcune limitazioni quali la bassa riproducibilità e quindi risultati a volte inconsistenti**

**Questi valori sono confirmatori di xerostomia, se in presenza dei sintomi specifici di xerostomia**

**E' importante determinare i volumi in entrambe le condizioni perché la secrezione salivare "a riposo" può essere diminuita nonostante un normale volume dopo la stimolazione**

# Scintigrafia con tecnezio

The diagnostic value of technetium 99m pertechnetate salivary gland scintigraphy in patients with certain salivary gland diseases.

Wu CB, Oral Maxillofac Surg. 2015

99mTc è assorbito e secreto dalle cellule epiteliali duttali e quindi presente nella saliva

Ghiandole salivari danneggiate non sono in grado di secernere il tecnezio che rimane intrappolato nella ghiandola

**I limiti della metodica includono la mancanza di standardizzazione, bassa risoluzione spaziale, nona data per la valutazione di modifiche morfologiche e scarsa specificità**

# **ecografia**

**Ecografia è la metodica standard nella diagnostica del parenchima delle ghiandole salivari, dimensioni, caratteristiche di ecogenicità e la definizione della architettura interna**

**I limiti della metodica nel predire e /o diagnosticare la xerostomia sono numerosi ed includono:  
operatore-dipendenza,  
non visualizzazione del lobo profondo  
non precisa valutazione delle dimensioni  
della ghiandola per la presenza della mandibola**

## TC

**La ghiandola parotide normale è visibile come un tessuto “fatty” incapsulato in una densa capsula, ma i dotti non sono visualizzati**

**I limiti di questa metodica sono numerosi:  
Alta densità del parenchima dopo 45 Gy  
Inaccurata indicazione di un progressivo danno da radiazioni**



# RM

RM ad alta risoluzione è un metodo non invasivo per la valutazione delle modifiche radio-indotte del parenchima ghiandolare, anche precoci, dopo due settimane di trattamento

**Collegare le caratteristiche morfologiche del parenchima ghiandolare con l'attività secretoria non è facile, anche con metodiche raffinate quali la RM, 3D MR scialografia e scintigrafia, specialmente durante la fase di infiammazione acuta della ghiandola.**

ASTREINIDOU, Int J Radiat Oncol Biol Phys. 2007

Unfortunately, it was found that pre- irradiation MR sialography could not help to predict the severity of radiation-induced xerostomia

dy.

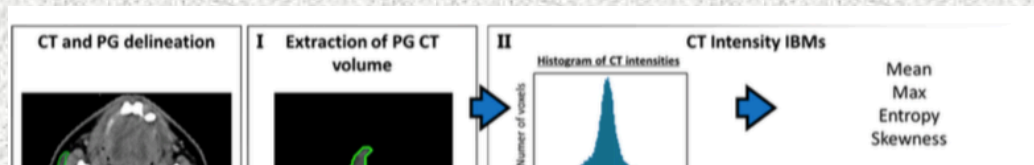
# CT image biomarkers to improve patient-specific prediction of radiation-induced xerostomia and sticky saliva

Lisanne V. van Dijk<sup>a,\*</sup>, Charlotte L. Brouwer<sup>a</sup>, Arjen van der Schaaf<sup>a</sup>, Johannes G.M. Burgerhof<sup>b</sup>, Roelof J. Beukinga<sup>a</sup>, Johannes A. Langendijk<sup>a</sup>, Nanna M. Sijtsema<sup>a</sup>, Roel J.H.M. Steenbakkers<sup>a</sup>

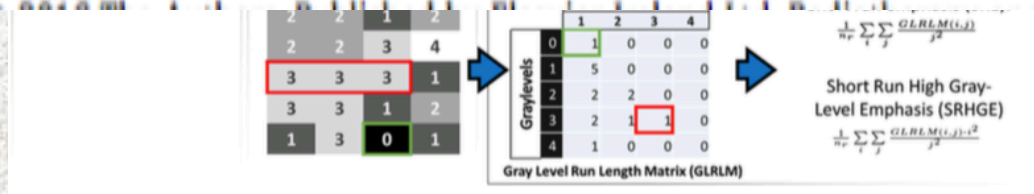
Radiotherapy and Oncology xxx (2016) xxx–xxx

The purpose is to improve prediction of XER<sub>12m</sub> and STIC<sub>12m</sub>

with patient-specific characteristics, based on CT image biomarkers (IBMs).



**Conclusion:** Prediction of XER<sub>12m</sub> and STIC<sub>12m</sub> was improved by including IBMs representing heterogeneity and density of the salivary glands, respectively. These IBMs could guide additional research to the patient-specific response of healthy tissue to radiation dose.



## Early prediction of radiotherapy-induced parotid shrinkage and toxicity based on CT radiomics and fuzzy classification

Marco Pota<sup>a,\*</sup>, Elisa Scalco<sup>b</sup>, Giuseppe Sanguineti<sup>c</sup>, Alessia Farneti<sup>c</sup>,  
Giovanni Mauro Cattaneo<sup>d</sup>, Giovanna Rizzo<sup>b</sup>, Massimo Esposito<sup>a</sup>

Artificial Intelligence in Medicine xxx (2017) xxx–xxx

“Early prediction of the shrinkage of the parotid gland at the end of RT. “

Infact, parotid shrinkage, and thus the variations of distance between the

**La predizione della xerostomia utilizzando “image-based features” è ancora un problema aperto, ci sono pochi lavori con risultati discordanti ma sembra una strada promettente**

**Xerostomia è associata con “oral discomfort” e dolore**

**Aumento delle carie dentali**

**Infezioni del cavo orale**

**Difficoltà nel parlare e nella deglutizione**

**Secchezza del cavo orale 95%**

**alterazione del gusto 90%**

**alterazione della fonazione 65%.**

**Carie dentali 45%**

**Xerostomia peggiora in maniera significativa  
la qualità della vita (QOL)**



## Metodi per una valutazione della Xerostomia post-radioterapia includono

1. Esame clinico
2. Misure obiettive quali la misurazione del flusso salivare
3. **Scale di valutazione Operator-rated outcomes (OROs)**

## The Radiation Therapy Oncology Group (RTOG) scoring criteria for acute radiation-induced salivary gland morbidity

Table 2. Acute and Late radiation Bone morbidity and salivary gland toxicity according to the Radiation Therapy Oncology Group scoring criteria (RTOG) [98]

	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
<i>Dry mouth</i>	Slight dryness of mouth; good response on stimulation	Moderate dryness of mouth;  poor response on stimulation	Complete dryness of mouth; no response on stimulation	Fibrosis	Death directly related to radiation late effects

## Metodi per una valutazione della Xerostomia post-radioterapia includono

1. Esame clinico
2. Misure obiettive quali la misurazione del flusso salivare
3. **Scale di valutazione Operator-rated outcomes (OROs)**

## Late radiation mandible and Salivary gland morbidity according to the Late Effects on Normal Tissue/Somatic Objective Management Analytic scale (SOMA scale)

Table 3 Late radiation Mandible and Salivary gland morbidity according to the Late Effects of Normal Tissue/Somatic Objective [99]  
Management Analytic scale\* (SOMA scale)

	Grade 1	Grade 2	Grade 3	Grade 4
<b>Salivary Gland</b>				
<b>SUBJECTIVE</b>				
Xerostomia	Occasional dryness	Partial but persistent dryness	Complete dryness, non-debilitating	Complete dryness, debilitating
<b>OBJECTIVE</b>				
Saliva	Normal moisture	Scant saliva	Absence of moisture, sticky, viscous saliva	Absence of moisture, coated mucosa
<b>MANAGEMENT</b>				
Xerostomia		Occasional saliva substitute Sugarless candy or gum, Sialogogues	Frequent saliva substitute or water Sugarless candy or gum, Sialogogues	Needs saliva substitute or water in order to eat Sugarless candy or gum, Sialogogues
<b>ANALYTIC</b>				
Salivary flow/quantity/ stimulation	76-95 % of pretreatment	51-75 % of pre-treatment	26-50 % of pre-treatment	0-25 % of pre-treatment

\*Instruction: Score the 9 SOM parameters with 1-4 (score 0 if there are no toxicities); total the score and divide by 9.

## Metodi per una valutazione della Xerostomia post-radioterapia includono

1. Esame clinico
2. Misure obiettive quali la misurazione del flusso salivare
3. **Scale di valutazione Operator-rated outcomes (OROs)**

**Common Terminology Criteria for Adverse Events v3.0 (CTCAE v3.0)** representing the first comprehensive, multimodality grading system to include both acute and late effects

Table 4. Dry-mouth toxicity according to the National Cancer Institute Common Toxicity Criteria (NCI-CTCAE) [88]

GRADE	Grade 1	Grade 2	Grade 3	Grade 4
Dry mouth	Symptomatic (e.g., dry or thick saliva) without significant dietary alteration; unstimulated saliva flow 0.2 ml/min	Moderate symptoms; oral intake alterations (e.g., copious water, other lubricants, diet limited to purees and/or soft, moist foods); unstimulated saliva 0.1–0.2 ml/min	Inability to adequately aliment orally; tube feeding or TPN indicated; unstimulated saliva 0.1 ml/min	--

# XEROSTOMIA

Xerostomia è associata ad una diminuzione del flusso salivare e modifica della Composizione della saliva



risultando in una **sensazione di bocca secca** e saliva vischiosa

**La sensazione di “bocca secca” compare quando il flusso salivare non stimolato si riduce del 45-50%**



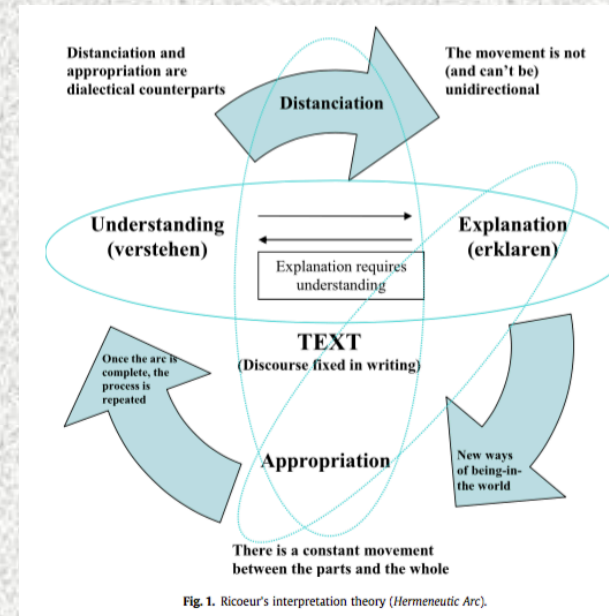
# Hermeneutic phenomenological interpretations of patients with head and neck neoplasm experiences living with radiation-induced xerostomia: The price to pay?

Andreas Charalambous<sup>a,b,c,\*1</sup>

European Journal of Oncology Nursing (2014)

Xerostomia is not a trivial condition for those suffering it. The insufficient attention to this side-effect can be partially attributed to the fact that xerostomia **is not classified as a life threatening side-effect**

The study aimed at exploring the **experiences of those living with xerostomia** and presumably those with more severe grades of xerostomia could describe the phenomenon in more depth.



Grade 2 xerostomia, two with Grade 3 and three patients were diagnosed with Grade 4 xerostomia.

## Suffering of the (physical) body

"It was like living the same bad dream over and over again, the dryness was killing me, I had to drink water all the time just to avoid that annoying feeling of stickiness and sand-like feeling and taste in my mouth ... and then there was the pain ... the persistency was nerve breaking". (Female, 55)

"I had never experienced anything quite like this before ... it was an awkward situation, wanting to swallow and not being able to ... it was almost as if someone was holding me by the neck and drowning me, suffocating me ... it was intolerable and torturing..." (Female, 50)

## Fear of eating and drinking

"I lost the pleasure of eating anything ... the time for eating became such fearful experience for me ... pain was only one side of the coin ... eating for me was like trying to eat toasted bread without teeth or trying to eat crisps after been in the desert for three days without water..." (Female, 42)

## Absorbing the body's energy

*"Sleeping became a luxury for me, I often found myself awakening in the middle of the night by a disturbing inability to swallow, it sometimes felt that I had a knot in my throat, it was almost as if I were suffocating [...] once waken then I found it difficult to get back to sleep [...] eventually I became a lifeless person with no energy to do anything [...]" (Female 50)*

## Being withdrawn

*"[...] I did not see this coming, I was disappointed by how things progressed (i.e. excessive dryness that affected her ability to speak) as I saw my personal and social life deteriorating [...] I felt that [...] I had to settle with an important asset of my everyday living ... my communication with the outer world, my family, my friends, and my colleagues" (Female 47)*

*"It was not only the difficulty in speaking properly; having difficulties in eating and drinking drove me away from simple social events such as going out for a dinner with my friends, I really missed this, but I didn't see the point anymore" (Male 51)*



## Feeling despair for having to live with xerostomia

*"Coming to terms with xerostomia was one thing, but having to put up with it for the rest of my life ... scared me and made me sad [...], I was deeply disappointed and I felt there was nothing I could do" (Female 55).*

## Being emotionally drained

*"I was definitely depressed; I surely felt like that, I lost my eagerness to live ... living was about doing the things I liked and being with the people I loved, I think that I lost both, I was left with nothing, it was just me and my thoughts, it was not fair ... it drained all my energy" (Male 56)*

Similarly, on the same topic, the difficulty faced by the patients in accepting the changes inflicted by xerostomia had an emotional impact on their lives:

*"I gave it up ... I didn't feel and I was not willing to do anything, I didn't recognize myself anymore, this thing had left a shell of my previous self, a self that I despised [...]" (Female 39)*



## Disappointment from the ineffective treatments

*"I had been taking this medicine (i.e. pilocarpine) for 3 days, I had seen some improvement in my dry mouth, but then I had to face the intense sweating which made my life difficult when I was at work or in a meeting, not to mention the need to wake up in the middle of the night and change my sheets and have a shower as a result of a sweat bath caused by the drug" (Male 49)*

On the same topic a female patient (42) narrated the following:

*"Drugs for xerostomia were a joke, they had no effect at all and when they did it only lasted for a while and then the wheel was again set in motion with the same effects. This spray (i.e. artificial saliva) made me nauseous, every time I used it I wanted to throw up, I preferred the xerostomia to that"*

**Patients narrated that often their professional carers viewed theirs symptoms merely as “the price to pay for cancer cure”.**

### **Being ignored**

*“Dry mouth was only a small price for you to pay, considering that we managed to treat cancer for you ... this was what my physician told me when I kept complaining about the persistent and discomforting side-effects of radiation. Small price...? It was easier said than done and living with this (xerostomia) was really a living nightmare that pushed me to my limits [...]” (Male 49)*

### **Being frustrated**

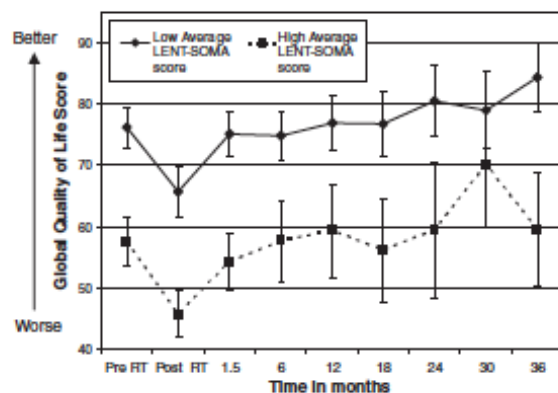
*“I was angry with her [physician], as I only heard that I had to be patient and accept things as they were ... the new order of things ... this was my life we were talking about [...] no real solutions for a real problem ... just like “bandages for an amputated leg” [...] ... my life was not the same anymore ... and there were moments that these became unbearable” (Female 39)*

## Comparison of patient-reported late treatment toxicity (LENT-SOMA) with quality of life (EORTC QLQ-C30 and QLQ-H&N35) assessment after head and neck radiotherapy

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*Radiotherapy and Oncology 97 (2010) 270–275*

**Materials/methods:** LENT-SOMA and EORTC QLQ-C30 patient questionnaires were prospectively completed by 220 head and neck cancer patients over 3 years and 72 completed EORTC QLQ-H&N35 questionnaires at 2 years post-radiotherapy.



**Conclusions:** LENT-SOMA patient questionnaire results agreed well with those from the EORTC QLQ-H&N35 questionnaire for toxicity items where they could be compared explicitly, particularly for subjective endpoints. Patient-reported late toxicity had a negative impact on quality of life. The LENT-SOMA patient questionnaire is both reliable and sensitive to differences between patients treated with different modalities. A patient-based questionnaire is an important contributor to capturing late radiotherapy effects.

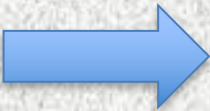
© 2010 Published by Elsevier B.V. Radiotherapy and Oncology 97 (2010) 270–275



## Metodi per una valutazione della Xerostomia post-radioterapia includono

1. Esame clinico
2. Misure obiettive quali la misurazione del flusso salivare
3. **Scale di valutazione Patient-rated outcomes (PROs)**

## Patient-rated xerostomia (EORTC QLQ-HN35)



	Scale name	Number of items	Item range	QLQ-H&N35 item numbers
<b>Symptom scales / items</b>				
Pain	HNPA	4	3	1 – 4
Swallowing	HNSW	4	3	5 – 8
Senses problems	HNSE	2	3	13,14
Speech problems	HNSP	3	3	16,23,24
Trouble with social eating	HNSO	4	3	19 – 22
Trouble with social contact	HNSC	5	3	18,25 – 28
Less sexuality	HNSX	2	3	29,30
Teeth	HNTE	1	3	9
Opening mouth	HNOM	1	3	10
Dry mouth	HNDR	1	3	11
Sticky saliva	HNSS	1	3	12
Coughing	HNCO	1	3	15
Felt ill	HNFI	1	3	17
Pain killers	HNPk	1	1	31
Nutritional supplements	HNNU	1	1	32
Feeding tube	HNFE	1	1	33
Weight loss	HNWL	1	1	34
Weight gain	HNWG	1	1	35



**EORTC**  
European Organisation for Research  
and Treatment of Cancer

*QoL*

EORTC Quality of Life

Head & Neck cancer module: QLQ-H&N35



**Metodi per una valutazione della Xerostomia post-radioterapia includono**

- 1. Esame clinico**
- 2. Misure obiettive quali la misurazione del flusso salivare**
- 3. Scale di valutazione Patient-rated outcomes (PROs)**

**Xerostomia Quality of Life (XeQoL),**

**Short Form-8 (SF-8)**

**Xerostomia severity scale (XSS) from 0-10.**

# Patient-rated outcomes (PROs)

## Assessment of radiation-induced xerostomia: validation of the Italian version of the xerostomia questionnaire in head and neck cancer patients

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Bruno Fattori · Guido Sotti

Support Care Cancer

DOI 10.1007/s00520-014-2438-2

**Table 2** Psychometric properties of the eight items of XQ-1

Item label	Text (abbreviated)	Factor loading	Item total correlation	Cronbach's alpha when item deleted
XQ1	Difficulty in talking due to dryness	0.81	0.75	0.92
XQ2	Difficulty in chewing due to dryness	0.85	0.79	0.92
XQ3	Difficulty in swallowing solid food due to dryness	0.85	0.79	0.92
XQ4	Sleeping problems due to dryness	0.66	0.58	0.94
XQ5	Dryness when eating	0.87	0.82	0.92
XQ6	Dryness while not eating	0.81	0.75	0.92
XQ7	Sip liquids to aid swallowing food	0.87	0.82	0.92
XQ8	Sip liquids for oral comfort	0.86	0.82	0.92

**Conclusions** The Italian version of XQ has excellent psychometric properties and can be used to evaluate the impact of emerging radiation delivery techniques aiming at preventing xerostomia.

## Xerostomia Quality of Life Scale (XeQoLS) questionnaire: validation of Italian version in head and neck cancer patients

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Roberta De Majo<sup>1</sup> · Andrea Rampini<sup>1</sup> · Pietro Giovanni Gennari<sup>1</sup> · Paola Pernici<sup>1</sup>

Radiol med

DOI 10.1007/s11547-017-0798-7

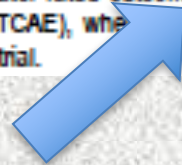
**Results** The questionnaire was considered simple by the patients. The clarity of the instructions and the easiness to answer questions had a mean value of 4.5 ( $\pm$  0.71) on a scale from 1 to 5.

**Conclusion** A valid multi-step process led to the creation of the final version of the XeQoLS-IT, a suitable instrument for the perception of xerostomia in patients treated with RT.

**Oral toxicity management in head and neck cancer patients treated with chemotherapy and radiation: Xerostomia and trismus (Part 2). Literature review and consensus statement.**

**M Buglione Crit Rev Oncol Hematol. 2016**

Clusters	Phase	Description	Whom is it in charge of?
	Definition	CTCAE definition: Xerostomia or dry mouth. A disorder characterized by reduced salivary flow in the oral cavity.	
1.	General statement	Xerostomia is defined as the decrease in salivary output (hypo-salivation) and a change in salivary composition, resulting in the sense of a dry mouth and sticky saliva. Xerostomia has a significant AE on health-related quality of life.	<ul style="list-style-type: none"><li>• Clinical oncologist</li><li>• Nurse</li></ul>
2.	Assessment scale	A Operator-rated outcome (ORO) grading scale is recommended in the clinical practice (e.g. NCI- CTCAE), while a PRO-grading scale (e.g. EORTC QLQ) needs to be added in the clinical trial.	<ul style="list-style-type: none"><li>• Clinical oncologist</li><li>• Nurse</li></ul>





Associazione Italiana  
**Radioterapia Oncologica**  
Gruppo Interregionale  
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## Le terapie di supporto in Radioterapia: **Verso una Guida Pratica**

Lunedì 4 Dicembre 2017  
Centro Studi Cardello  
Via del Cardello 24 – Roma

# ***Grazie per l'attenzione***

## Tossicità nei trattamenti del distretto Iesta-Collo

### **Xerostomia**

### **Cenni di patogenesi e Strumenti di valutazione**

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