

XXV CONGRESSO NAZIONALE

AIRO 2015

PALACONGRESSI - Rimini, 7-10 novembre

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Orbassano
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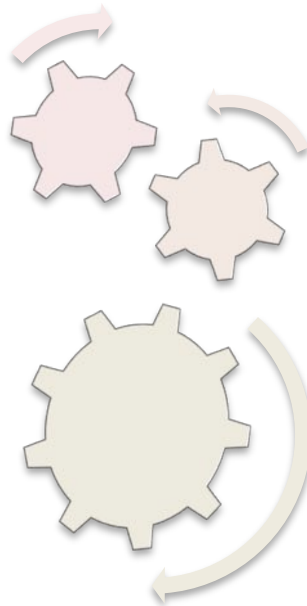
**Analisi della funzionalità delle ghiandole parotidi
mediante scintigrafia salivare dopo IMRT nei pazienti
affetti da neoplasia delle testa e del collo:
correlazione tra dati dosimetrici e parametri
semiquantitativi di secrezione salivare residua**

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- Xerostomia is one of the most common toxicities after radiation therapy for head and neck (H&N) cancer
- IMRT offers a way to effectively reduce the adsorbed dose to the salivary glands, particularly to parotid glands (PGs) with generation of steep dose gradient



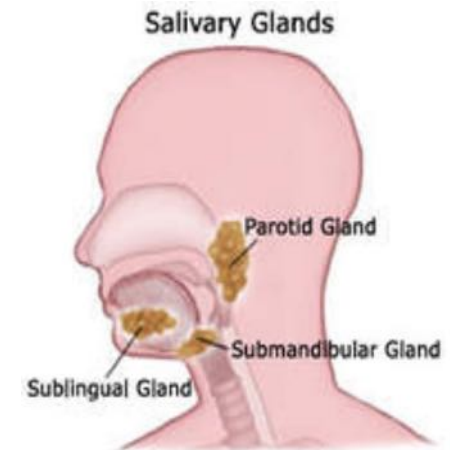
- IMRT target delineation in H&N cancer is complex and often the PGs are inevitably irradiated because of the extensiveness of tumor, or the anatomic location of the glands
- at least preservation of the parotid contralateral to the disease is possible
- Set-up errors and PGs shrinkage during IMRT may induced to unwanted PGs irradiation
- IMRT does not necessarily improve the patient-reported xerostomia

Salivary gland scintigraphic examination is an objective method useful to evaluate salivary glands function

In this preliminary study we evaluated and compared PGs function before and after IMRT assessed by salivary gland scintigraphy

Salivary gland scintigraphic examination is an objective method useful to evaluate salivary glands function

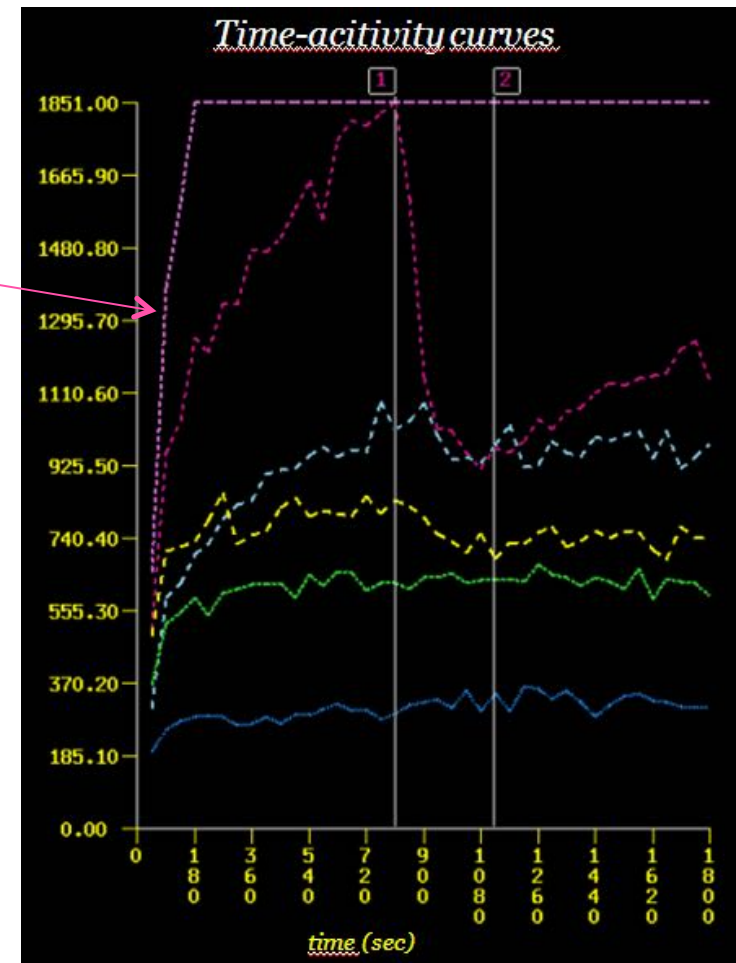
- Semi-quantitative analysis of ^{99m}Tc -pertechnetate salivary gland scintigraphy is a non invasive investigation useful in the evaluation of salivary gland function
- This technique provides images of the parotid and submandibular glands
- Physiologic intervention by administration of a sialogogue such as lemon juice provides information on the salivary glands function
- This technique provides 2 parameters of function: **uptake rate parameter** and **washout fraction parameter** providing information that could be useful to categorize the effects of insults to the salivary glands



Salivary gland scintigraphic examination is an objective method useful to evaluate salivary glands function

The uptake rate parameter:

measure of how well the salivary glands could extract the radiotracer from the peripheral venous circulation, with a mechanism of the ion-pump. It is represented from the early rising part of the time-activity curve; diseased salivary gland show a slowly rising curve with a resulting decreased slope, compared with normal PGs.

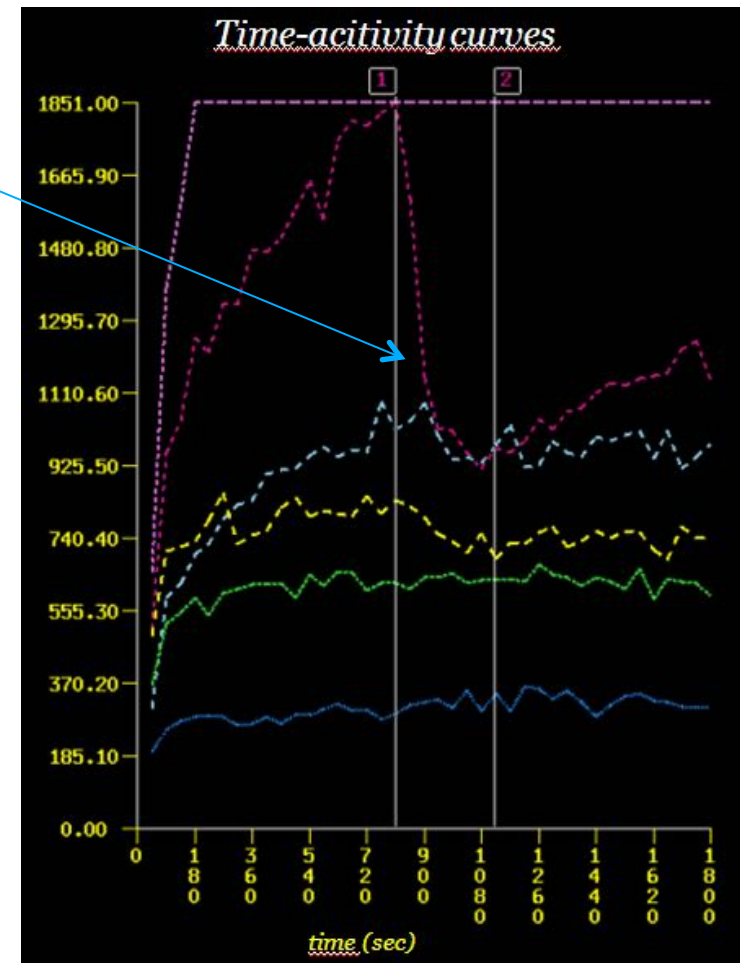


Salivary gland scintigraphic examination is an objective method useful to evaluate salivary glands function

The washout fraction parameter

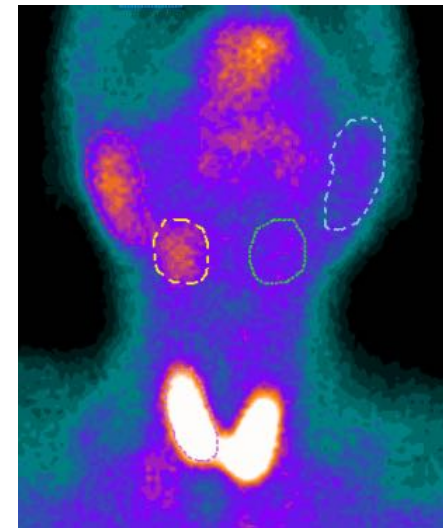
$$\frac{\text{excreted saliva}}{\text{saliva persisting inside the glands}}$$

obtained measuring saliva radioactivity after ingestion of lemon juice, as response to the secretory acid stimulus. The plateau of the time-activity curves was reached 6 and 10 min after injection, and radioactivity in the salivary gland was located in 2 separate pools: 1) mobilizable one; 2) a non-mobilizable one remaining in the parenchymal cells.



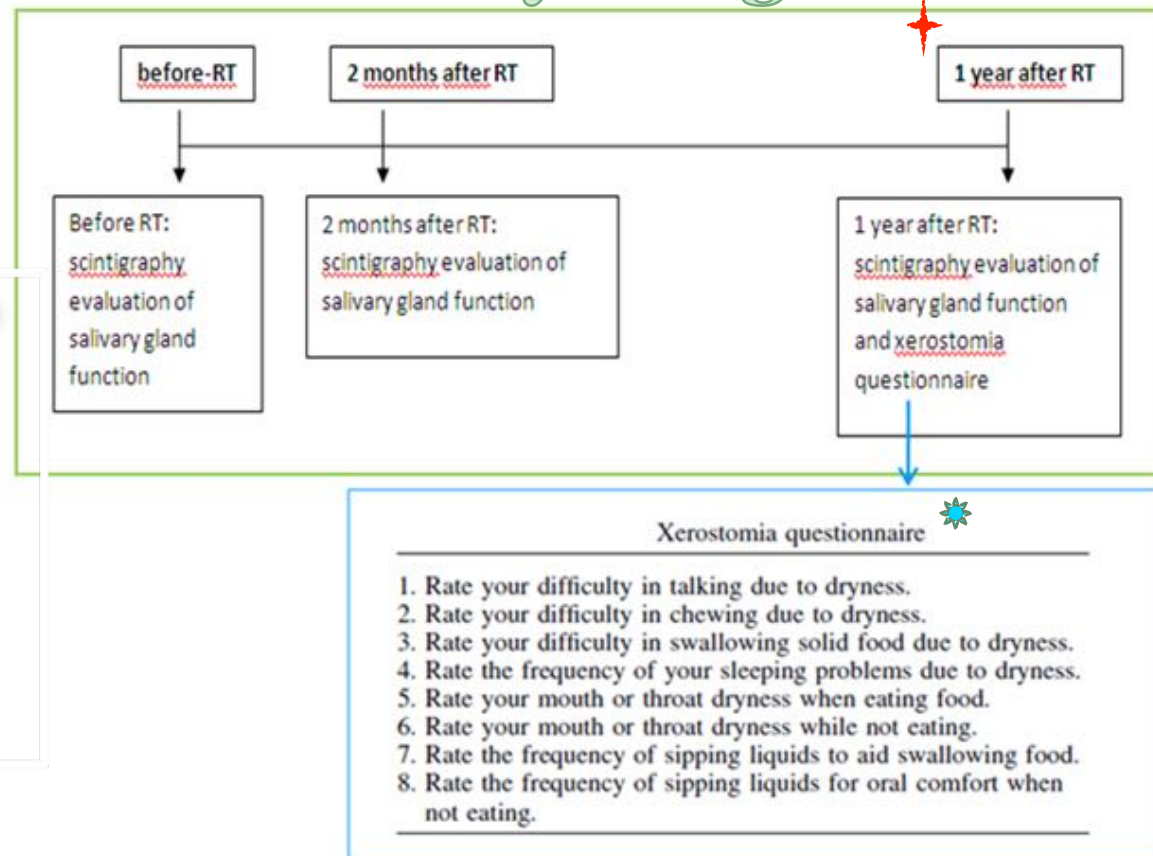
Salivary gland scintigraphic examination is an objective method useful to evaluate salivary glands function

- Imaging is performed using a dual heads gamma-camera
- The patient is supine, and the camera was positioned for an anterior head-and-neck projection.
- Dynamic imaging is performed starting immediately after a bolus intravenous injection of 185 MBq (5 mCi) 99mTc-sodium pertechnetate.
- Imaging continued for 30 min after injection.
- At 15 min after injection, each patient drinks the juice of a lemon, using a straw and without moving, while imaging is continued.
- Regions of interest (parotid glands +/- submandibular glands) were drawn on the dynamic images.
- Time-activity curves were generated for each region.



**In this preliminary study we
 evaluated and compared PGs
 function before and after IMRT
 assessed by salivary gland
 scintigraphy**

Study design



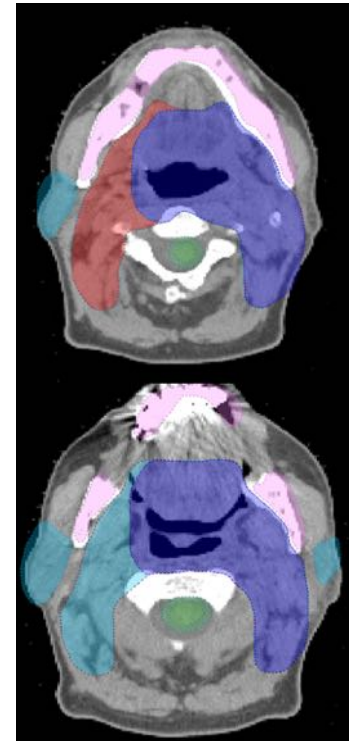
One year after IMRT → most studies focusing on the recovery of the salivary glands after curative radiotherapy had only a follow-up period of 12 months.

Braam PM, Roesink JM, Moerland MA, Raaijmakers CP, Schipper M, Terhaard CH: **Long-term parotid gland function after radiotherapy.** *Int J Radiat Oncol Biol Phys* 2005, 62:659-664

Jabbari SB, Kim HM, Feng M, Lin A, Tsien C, Elshaikh M, Terrel JE, Murdoch-Kinch C, and Eisbruch A: **Matched case-control study of quality of life and xerostomia after intensity-modulated radiotherapy or standard radiotherapy for head-and-neck cancer: initial report.** *Int. J. Radiation Oncology Biol. Phys.*, Vol. 63, No. 3, pp. 725-731, 2005

Eisbruch A, Kim HM, Terrell JE, et al. **Xerostomia and its predictors following parotid-sparing irradiation of head and neck cancer.** *Int J Radiat Oncol Biol Phys* 2001;50:695-704.

- From May 2011 to September 2013, **four** patients with diagnosis of H&N cancer underwent salivary glands scintigraphy (SGS) before, 2 months and one year after IMRT respectively, with appropriate medical release
- After immobilization a planning CT was performed (3 mm); standard protocols were followed in delineating the regions of interest and OARs (RTOG 0225)
- The prescription dose was 69.9 Gy to PTV1 (T+N) with simultaneous integrated boost technique and 60 Gy to PTV2 (subclinical disease) in 33 fractions or 70 Gy with standard schedule, administered to 1 and 3 patients respectively
- IMRT was based on the step-and-shoot approach with 7-9 fields, and 6 MV photons of LINAC (Sinergy Platform; Elekta Atlanta, GA, USA) were used
- In all patients an internal quality assurance adaptive-radiotherapy off-line protocol [1] was followed
- **The mean dose of at least one parotid gland was limited to 26 Gy without compromising the PTV coverage**



[1] Reali A, Anglesio SM, Mortellaro G, Allis S, Bartoncini S, Arcadipane F, Ruo Redda MG. Volumetric and positional changes of planning target volumes and organs at risk using computed tomography imaging during intensity-modulated radiation therapy for head-neck cancer: an "old" adaptive radiation therapy approach. Radiol Med. 2014 Sep;119(9):714-20.



Analisi della funzionalità delle ghiandole parotidi mediante scintigrafia sequenziale salivare dopo IMRT nei pazienti affetti da neoplasia delle testa e del collo: studio preliminare sulla correlazione tra dati dosimetrici e parametri quantitativi di secrezione salivare residua

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QUANTEC: ORGAN-SPECIFIC PAPER

Head and Neck: Parotid

RADIOTHERAPY DOSE-VOLUME EFFECTS ON SALIVARY GLAND FUNCTION



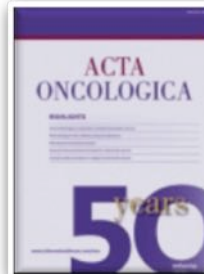
JOSEPH O. DEASY, PH.D.,* VITALI MOISEENKO, PH.D.,† LAWRENCE MARKS, M.D.,‡
K. S. CLIFFORD CHAO, M.D.,§ JIHO NAM, PH.D.,‡ AND AVRAHAM EISBRUCH, M.D.¶

*Department of Radiation Oncology, Washington University School of Medicine and Alvin J. Siteman Cancer Center, St. Louis, MO; †Department of Medical Physics, British Columbia Cancer Agency-Vancouver Cancer Center, Vancouver, BC, Canada; ‡Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, NC; §Department of Radiation Oncology, Columbia School of Medicine, New York, NY; ¶Department of Radiation Oncology, University of Michigan School of Medicine, Ann Arbor, MI

Int. J. Radiation Oncology Biol. Phys., Vol. 76, 2010

8. RECOMMENDED DOSE-VOLUME LIMITS

For complex partial volume RT patterns (*e.g.*, intensity-modulated RT), the mean dose to each parotid gland should be kept as low as possible, consistent with the desired clinical target volume coverage. A lower mean dose to the parotid gland usually results in better function, even for relatively low mean doses (<10 Gy). Similarly, the mean dose to the parotid gland should still be minimized, consistent with adequate target coverage, even if one or both cannot be kept to a threshold of <20 or <25 Gy. Published variations in response among different patient cohorts were probably related to the lack of an accurate model that correctly includes the effects of multiple salivary glands and intragland sensitivity variations. When it can be deemed oncologically safe, submandibular gland sparing to modest mean doses (<35 Gy to see any effect) might reduce xerostomia symptoms.



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

Acta Oncologica

Ivo Beetz, Roel J. H. M. Steenbakkers, Olga Chouvalova, Charles R. Leemans, Patricia Doornaert, Bernard F. A. M. van der Laan, Miranda E. M. C. Christianen, Arjan Vissink, Henk P. Bijl, Peter. van Luijk & Johannes A. Langendijk

Acta Oncologica, 2014; 53: 597-604

Based on the findings of the present study, it appears that with IMRT it is more difficult to spare the parotid glands than with 3D-CRT, which is actually not true.

QUANTEC criteria in this study could only be met in a minority of patients. New radiation delivery techniques to further reduce the dose to the relevant salivary glands are therefore required, which we suggest as a topic for future research.



***Analisi della funzionalità delle ghiandole parotidi
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RESEARCH

Open Access



Parotid gland-recovery after radiotherapy in the head and neck region - 36 months follow-up of a prospective clinical study

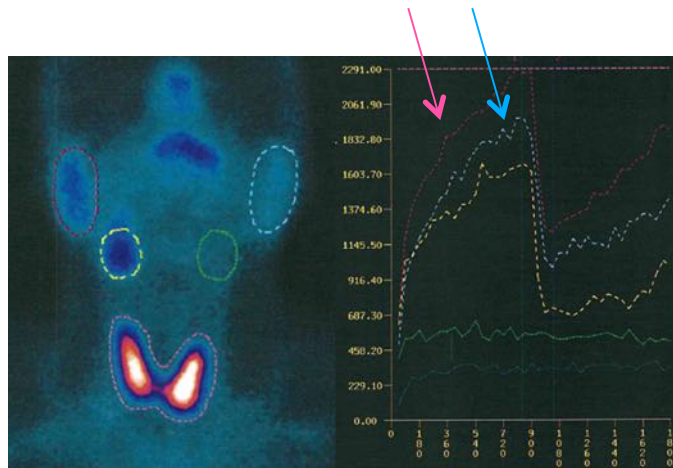
Radiation Oncology 2011

Jeremias Hey¹, Juergen Setz¹, Reinhard Gerlach², Martin Janich², Guido Hildebrandt⁴, Dirk Vordermark², Christian R Gernhardt³ and Thomas Kuhn^{4*}

By using IMRT a mean parotid gland dose < 26 Gy was reached in 12/15 patients (80%), and a dose range > 26 to 40 Gy in 3/15 patients (20%). Parotid-gland-sparing up to mean doses of 26 Gy proved to be a reliable method to avoid distinct long lasting xerostomia.

In this preliminary study we evaluated and compared PGs function before and after IMRT assessed by salivary gland scintigraphy

We obtained an appropriate sparing of the contralateral PG in 3 patients with a $D_{\text{mean}} \leq 26$ Gy (mean value 24.99 Gy, range \rightarrow 23.27 – 26.1 Gy); in only one the IMRT sparing of the contralateral PG was unsatisfactory with a $D_{\text{mean}} = 29.3$ Gy

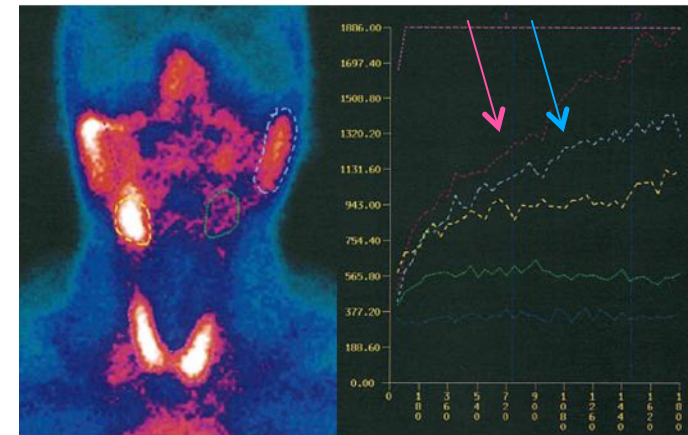


SGS before
IMRT

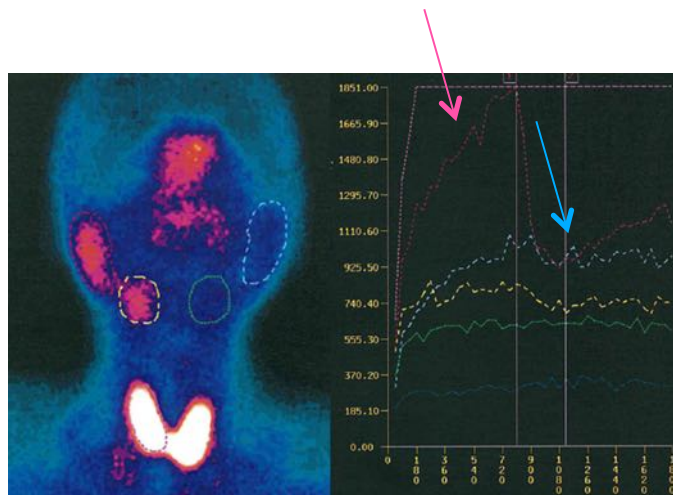
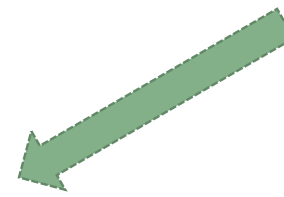
Curva attività/tempo

Parotide destra
Parotide sinistra
Sottomandibolare destra

Sottomandibolare sinistra
Tiroide
Background

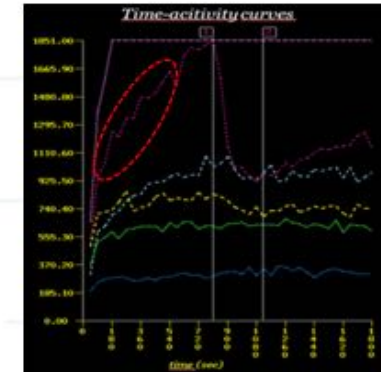
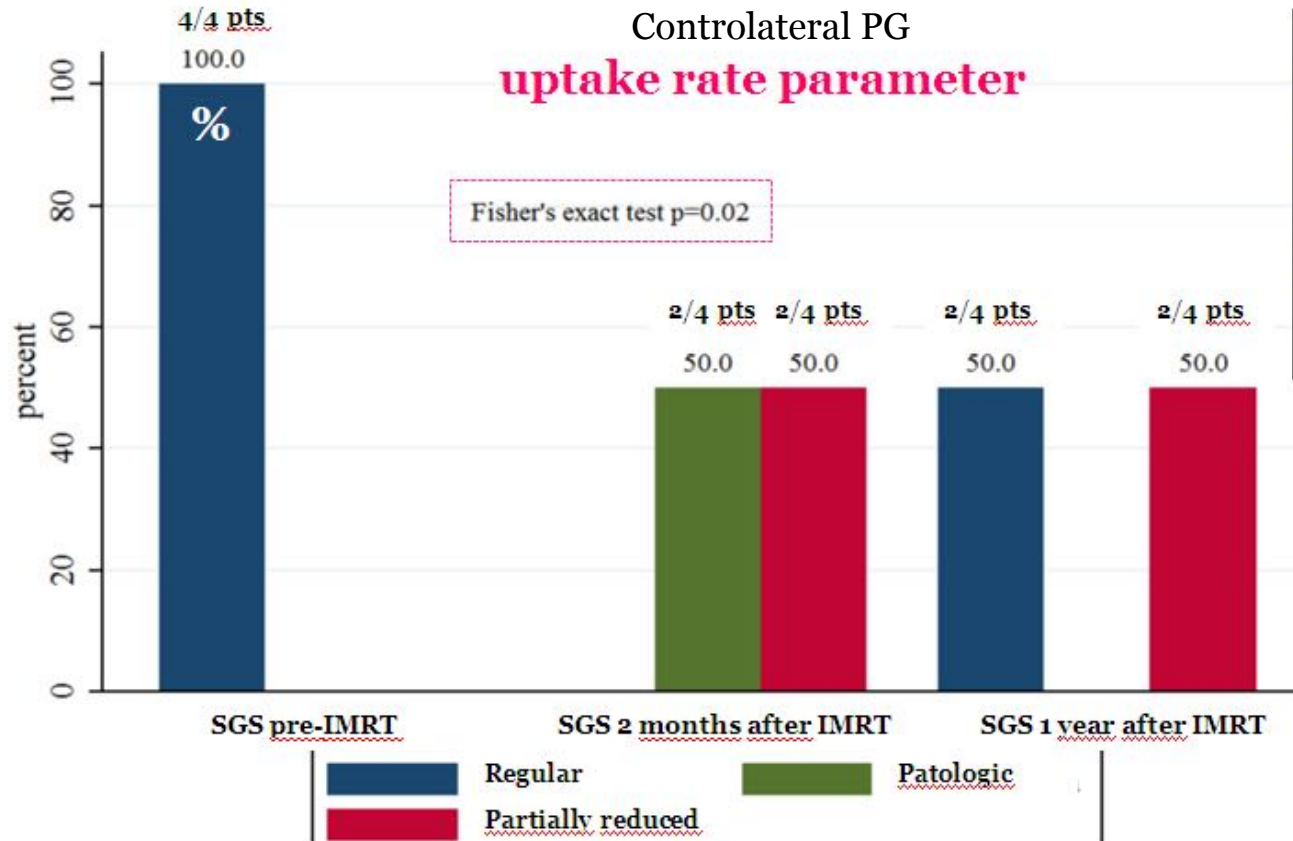


SGS 2 months
after IMRT

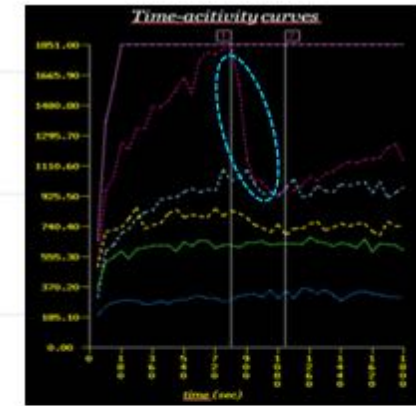
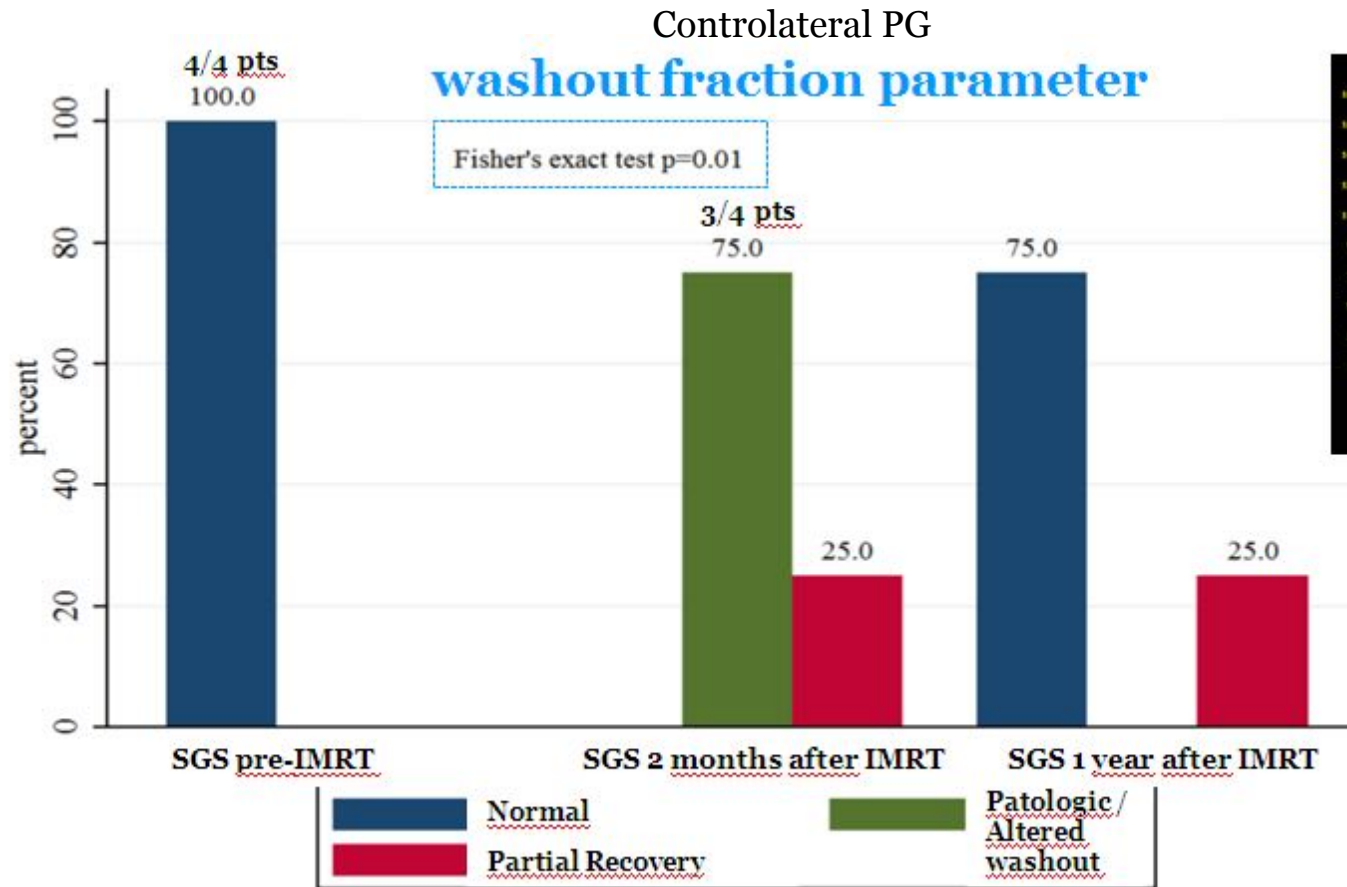


SGS one year
after IMRT

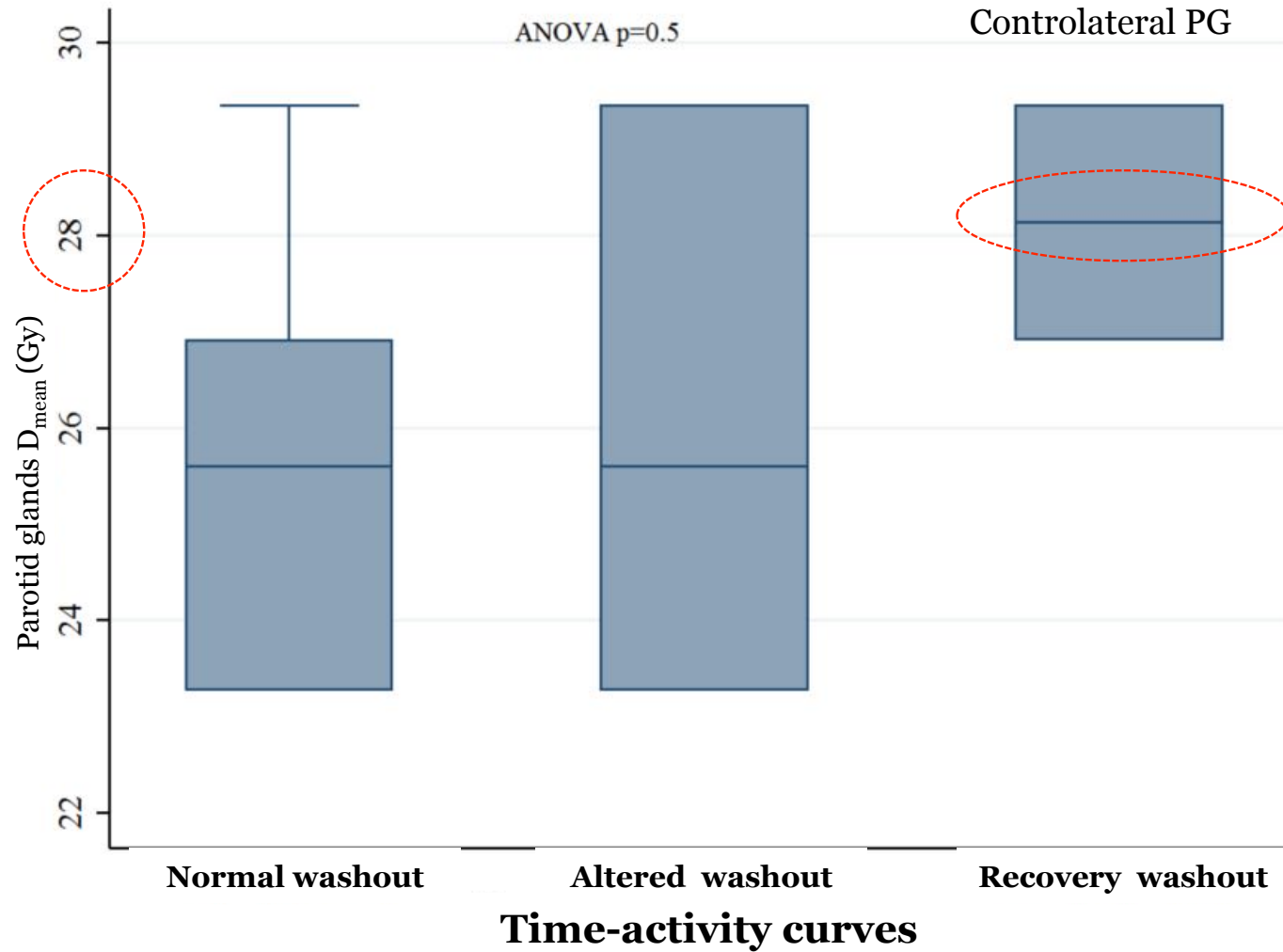
In this patient left PG was irradiated



There is no correlation between the level of impairment uptake at 2 months or 1 year after IMRT: for example 1 patient with pathological uptake at 2 months had complete recovery after 1 year, ecc. There is no correlation with fractionation schedule



There is no correlation between the level of impairment washout at 2 months or 1 year after IMRT. There is no correlation with fractionation schedule



**In this preliminary study we evaluated and compared
PGs function before and after IMRT assessed by
salivary gland scintigraphy**

**... and from subjective/quality of life
(QOL) point of view?**

Xerostomia questionnaire

1. Rate your difficulty in talking due to dryness.
2. Rate your difficulty in chewing due to dryness.
3. Rate your difficulty in swallowing solid food due to dryness.
4. Rate the frequency of your sleeping problems due to dryness.
5. Rate your mouth or throat dryness when eating food.
6. Rate your mouth or throat dryness while not eating.
7. Rate the frequency of sipping liquids to aid swallowing food.
8. Rate the frequency of sipping liquids for oral comfort when not eating.

- all patients referred an adequate salivary secretion
- remaining difficult to chewing and swallowing

CONSIDERATIONS



- **IMRT effectively reduces the dose to salivary glands without compromising the prescribed target dose**
- **Salivary glands scintigraphy is useful in monitoring residual salivary flow after IMRT**
- **Mean doses ≤ 26 Gy to PGs significantly preserve salivary function**
- **Our preliminary clinical results show an unexpected sub-acute toxicity with a delayed recovery of the preserved parotid gland → interesting clinical data that may be considered in xerostomia patient's information before IMRT**





INTRODUCTORY PAPER

**QUANTITATIVE ANALYSES OF NORMAL TISSUE EFFECTS IN THE CLINIC
(QUANTEC): AN INTRODUCTION TO THE SCIENTIFIC ISSUES**

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AVI EISBRUCH, M.D.,[§] ANDREW JACKSON, PH.D.,^{||} LAWRENCE B. MARKS, M.D.,[¶]
RANDALL K. TEN HAKEN, PH.D.,[§] AND ELLEN D. YORKE, PH.D.,^{||}

From the *Departments of Human Oncology, Medical Physics, Biostatistics and Medical Informatics, University of Wisconsin School of Medicine and Public Health, Madison, WI; [†]Department of Radiation Oncology, University of Rochester Medical Center, Rochester, NY; [‡]Department of Radiation Oncology, Washington University, St. Louis, MO; [§]Department of Radiation Oncology, University of Michigan, Ann Arbor, MI; ^{||}Department of Medical Physics, Memorial Sloan Kettering Cancer Center, New York, NY; [¶]Department of Radiation Oncology, University of North Carolina at Chapel Hill, NC



▪ **Tumor coverage vs normal tissue risk**

- for most curative patients, a marginal miss is more serious than a NTC
- target coverage should generally not be compromised to reduce the normal tissue risks
- improved diagnostic imaging, immobilization and IG during RT → a more realistic PTV margin to be applied safely

▪ **Applicability to the children**

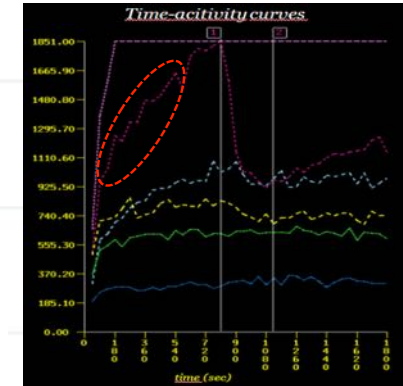
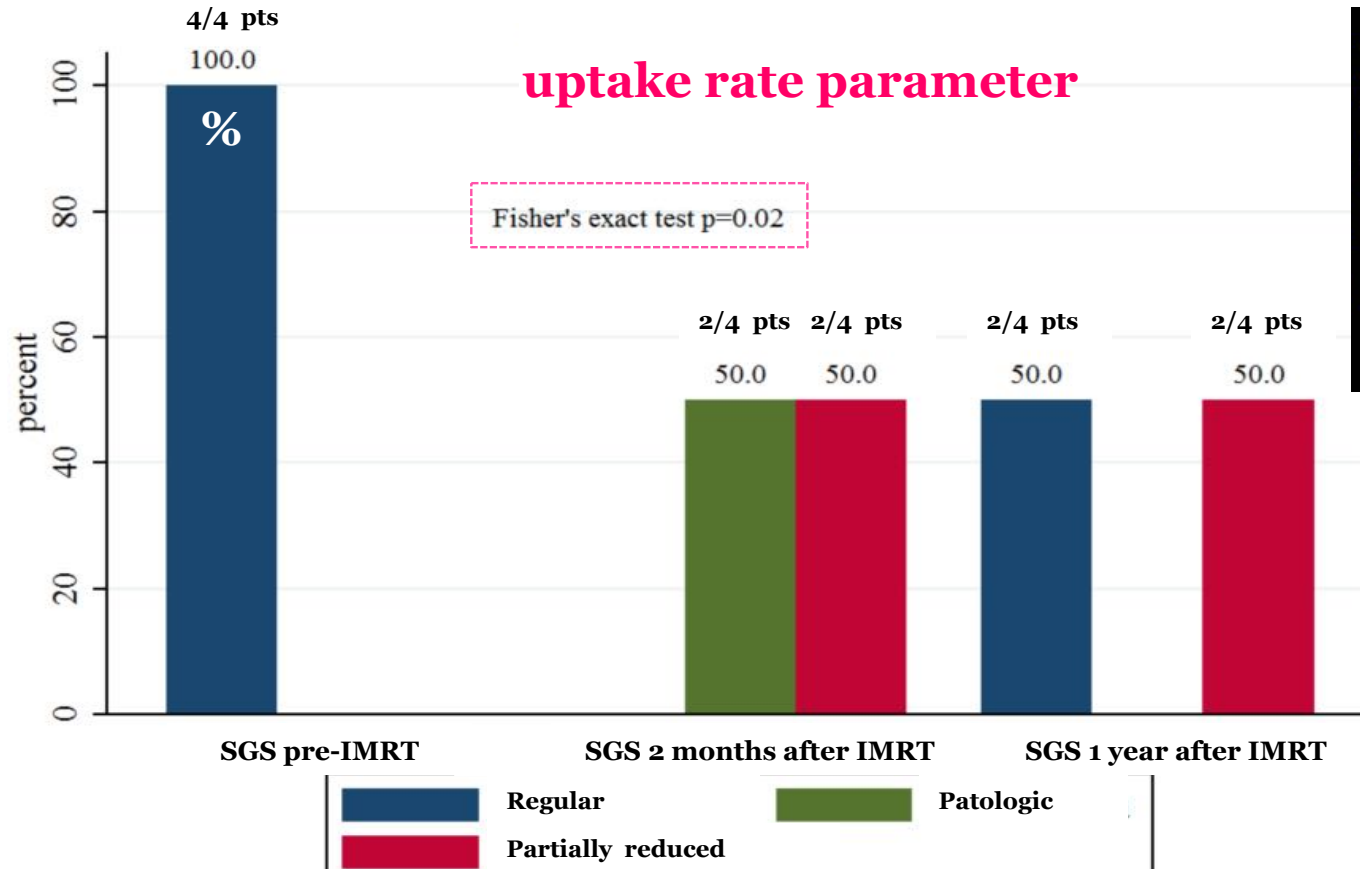
- generalizing data from adult to pediatric population is problematic and requires caution
- ideally, specific data from investigations on children should be used to predict risks in this population



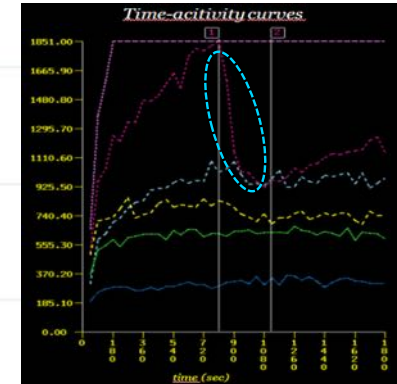
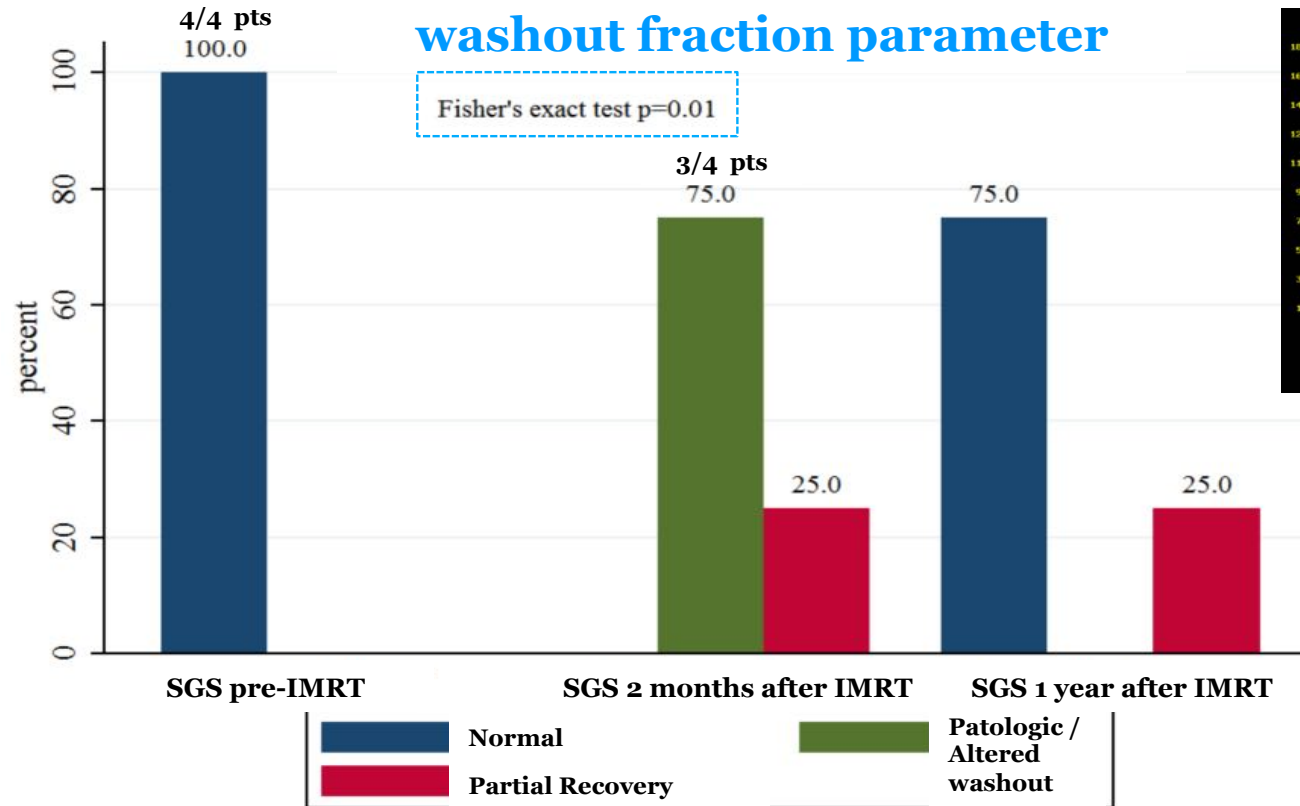
*L'amore per il proprio lavoro costituisce la migliore approssimazione della felicità sulla terra.
Ma questa è una verità che non molti conoscono.*

P. Levi

Grazie per l'attenzione



There is no correlation between the level of impairment uptake at 2 months or 1 year after IMRT: for example 1 patient with pathological uptake at 2 months had complete recovery after 1 year, another partial recovery ecc.



There is no correlation between the level of impairment washout at 2 months or 1 year after IMRT