

XXXII CONGRESSO NAZIONALE AIRO  
XXXIII CONGRESSO NAZIONALE AIRB  
XII CONGRESSO NAZIONALE AIRO GIOVANI

# AIRO2022

Radioterapia di precisione per un'oncologia innovativa e sostenibile

BOLOGNA, 25-27 NOVEMBRE  
PALAZZO DEI CONGRESSI

 Associazione Italiana  
Radioterapia e Oncologia clinica

 Società Italiana di Radiobiologia

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## **Radiation therapy-dependent oral mucositis: how the oral dysbiosis may predispose to opportunistic fungal infections and oral mucositis**

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## DICHIARAZIONE

Relatore: Dott.ssa Giulia Mascari

Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Consulenza ad aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Partecipazione ad Advisory Board **(NIENTE DA DICHIARARE)**
- Titolarità di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Altro

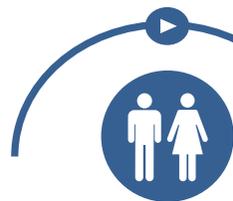


- ❖ Oral mucositis (OM) is a common acute side effect of radiation therapy (RT) in head-neck cancer patients (HNCs)
- ❖ There is a need of preclinical studies to delineate the mechanisms by which the oral dysbiosis may predispose to OM
- ❖ We performed an observational prospective study evaluating oral microbiota milieu pre/post/during head and neck radiotherapy



## PATIENTS AND METHODS

- ✓ HNCs > 18 years old
- ✓ naïve antibiotic therapy



## INCLUSION CRITERIA

## TREATMENT

RT or RT-CHT (30 fr.)  
(Surgery allowed)



## WITHDRAWALS

- ✓ oral swab for metagenomics and lipidomics (OMNIgene ORAL kit)
- ✓ an in vitro 3D tongue organoid model



## OM ASSESSMENT

- ✓ baseline, 7, 15 days from the beginning of RT
- ✓ end of RT
- ✓ 1 month, 3 months post-RT



“

**cis-platinum:**  
 40 mg/m<sup>2</sup>  
 1 day/wk for 6 wks

**Cetuximab (1):**  
 ❖ 400 mg/m<sup>2</sup>  
 pre-RT  
 ❖ 250 mg/mq  
 1 day/wk for 6 wks

”



## POPULATION

- ❖ From December 2020 - August 2022: 25 patients were recruited [18 M + 7 F; median age 70 (range 21-92)]
- ❖ 24 patients: squamous cell carcinoma (SCC) and 1 polymorphic adenoma of the minor salivary glands
- ❖ Clinical stages: T1 - T4N2bM0
- ❖ Medium Oral Dose: 27,23 Gy (range 0.19 - 63.19 Gy)



## PRELIMINARY RESULTS (11-2022)

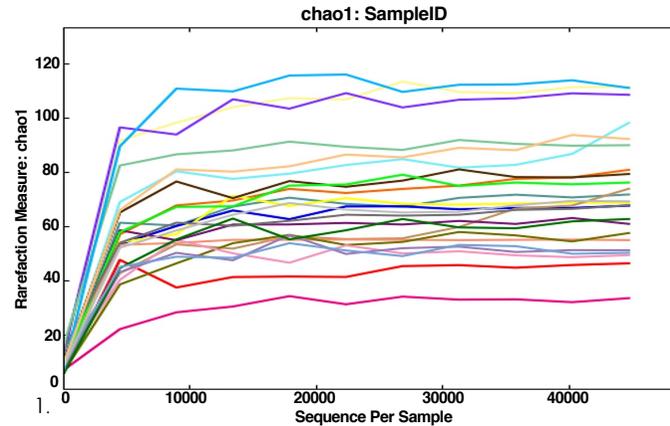
#	ID	AGE	SEX	TIME "0"	RT/RT-CHT	HPV	SURGERY	MEDIUM ORAL DOSE	TOXICITY CTCAE V5.0
1	34289	68	F	19/02/2021	RT - CDDP	-	-	40,84 Gy	Dysphagia G2 Voice alteration G3
2	39927	84	M	01/12/2020	RT	-	-	37,34 Gy	Dysphagia G1
3	40058	71	M	09/02/2021	RT	-	✓	32,87 Gy	Dysphagia G1
4	40084	73	F	08/02/2021	RT- CDDP	✓	-	54,65 Gy	Dry mouth G3 Dysphagia G1



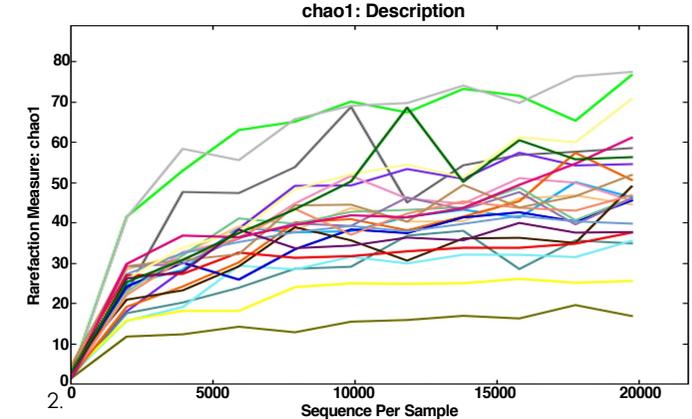
## PRELIMINARY RESULTS (11-2022)

- ❖ We collected tongue samples which were used for DNA extraction for 16S and 18S rRNA; sample richness is shown with chao diversity index (Fig.1-2)
- ❖ PCOA unweighted UniFrac analysis shows how that oral microbiome is organized in "stable orotypes" while distancing between pre and post RT is visible in weighted UniFrac analysis (Fig. 3-4)

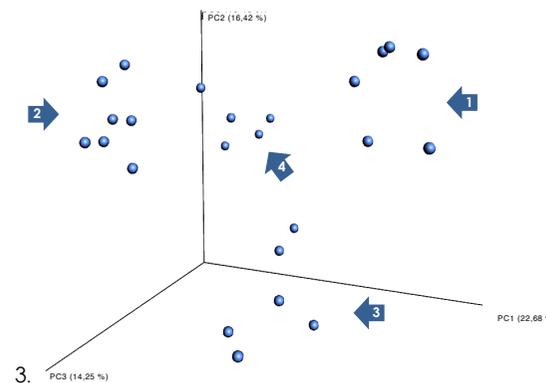
**16S Alpha diversity rarefaction plot**



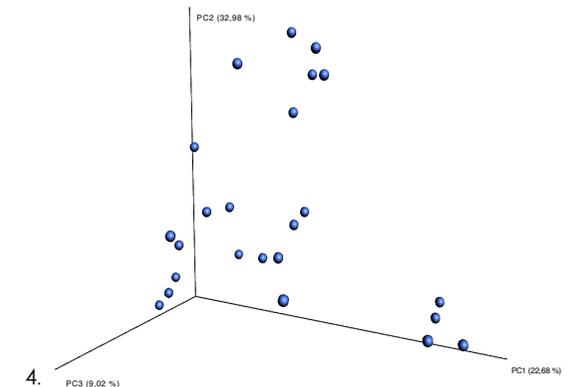
**18S Alpha diversity rarefaction plot**



**PCOA unweighted UniFrac analysis**



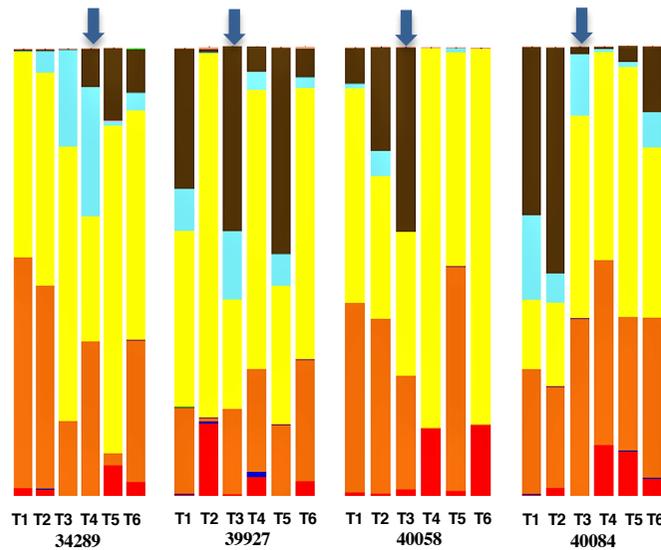
**PCOA weighted UniFrac analysis**





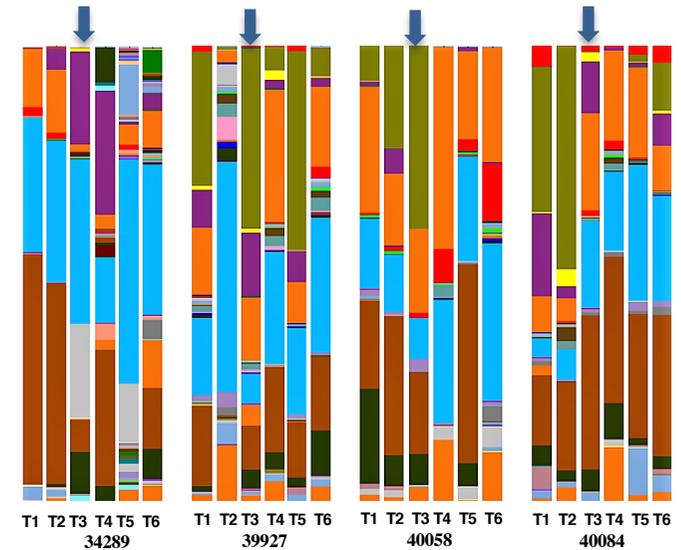
## PRELIMINARY RESULTS (11-2022)

### 16S Taxa summary bar plot



### 16S Taxa summary bar plot

- Bacteria:Actinobacteria
- Bacteria:Bacteria\_unclassified
- Bacteria:Bacteroidetes
- Bacteria:Candidate\_division\_SR1
- Bacteria:Elusimicrobia
- Bacteria:Firmicutes
- Bacteria:Fusobacteria
- Bacteria:Gemmatimonadetes
- Bacteria:Planctomycetes
- Bacteria:Proteobacteria
- Bacteria:Spirochaetae
- Bacteria:Synergistetes
- Bacteria:Tenericutes



- ❖ During RT, Bacteroides Phylum was reduced and in particular the Genus **Prevotella** (50% → 10%)
- ❖ Firmicutes Phylum increased, particularly the Genus **Streptococcus** (30 → 50%)
- ❖ 18S sequencing showed **Candida albicans** and **Aspergillus** increased colonization post-RT



## CONCLUSIONS

- ❖ These preliminary results underline an oral dysbiosis in the analysis of the 4 patients undergoing RT
- ❖ RT toxicity may trigger the appearance of opportunistic infections and oral dysbiosis by changing the composition of individual "orotypes"

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## GRAZIE PER L'ATTENZIONE