

# Management of Radiation Toxicities *Head & Neck Cancer*

**Dr Madhup Rastogi**

*MD, FICRO, UICCF (USA)*

*Vice President ICRO*

Prof & Head

Department of Radiation Oncology

RMLIMS, Lucknow

[drmadhup1@gmail.com](mailto:drmadhup1@gmail.com)

# **Role of Radiotherapy in Head and Neck cancers**

- Radical, Post op, Palliative
- RT/ CTRT
- Reirradiation

**Although radiotherapy offers immense benefit to the patient, it still causes unwanted short term & long-term sequelae.**

The dose of radiation and the amount of tissue volume exposed are the main risk factors for RIT.



**Therapeutic Window**

# Radiation Induced Side-effects/ toxicity

## Acute (early)

- Occurring within 90 days (few days to weeks)
- In tissues of rapid rate of turn over e.g. Skin, GI, hematopoietic

## Chronic (late)

- Appears months to years after the treatment
- In slowly proliferating tissues e.g. CNS, lung

### Acute (early)

- Radiation dermatitis
- Oral mucositis
- Dysphagia
- Pain

### Chronic (late)

- Fibrosis
- Xerostomia
- Trismus
- Lymphedema

# Adverse events classification/grading/scoring systems

- **WHO:** *easy to use in clinical setting*
- **RTOG/EORTC:** *earlier trials for mucositis & skin*
- **CTCAE:** *commonly used by modern clinical trials.*

# Common Terminology Criteria for Adverse Events (CTCAE)

Version 5.0

Published: November 27, 2017

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

- **Grade 0** No symptoms
- **Grade 1** Mild
- **Grade 2** Moderate
- **Grade 3** Severe
- **Grade 4** Life-threatening
- **Grade 5** Death

Grade 1	Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.
Grade 2	Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL*.
Grade 3	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self care ADL**.
Grade 4	Life-threatening consequences; urgent intervention indicated.
Grade 5	Death related to AE.

---

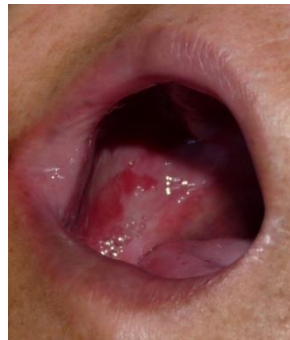
Note: Activities of Daily Living (ADL); \*Instrumental ADL refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.; \*\*Self care ADL refer to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not bedridden.

# Mucosal Toxicity

✓ Virtually all patients of HNC receiving Radiotherapy develop some degree (grades) of mucositis during their treatment.

Incidence of OM with RT	Grade 1 & 2	Grade 3 & 4
	85 – 100 %	25 – 45 %

*Trotti A et al, (2003)Radiother Oncol. 66:253–262*



Most important Limiting Factor

- **Compliance**

# Oral Mucositis

In general terms, mucositis is the inflammation of the mucous membrane of oral and oropharyngeal region.

If not detected or treated adequately can lead to pain, discomfort and inability to tolerate food or fluids, increased propensity for opportunistic infections in the mouth.

Poorly managed OM is one of the leading causes for *unplanned treatment interruptions* and therefore increasing overall treatment time.

Prolongation of overall treatment time adversely affects the *tumor control probability*.

It also increases the overall *cost* of the treatment.



# Risk Factors for OM

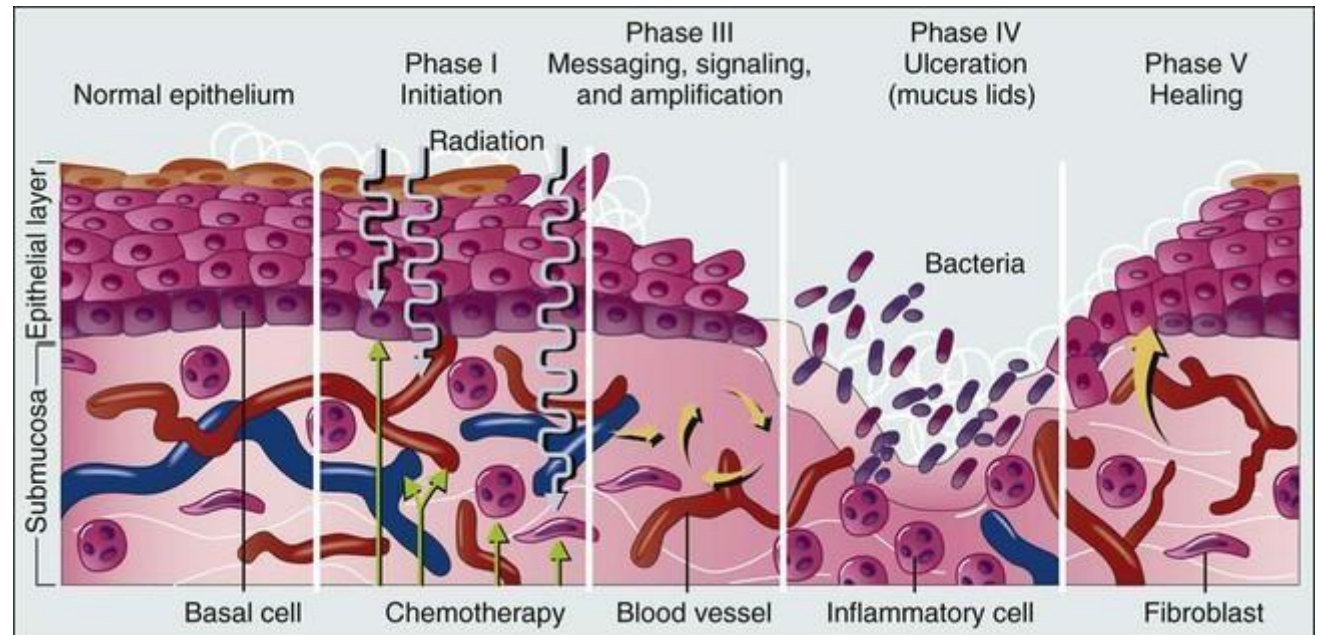
Influenced by a variety of patient- and treatment-related risk factors

- Gender & age
- Inadequate oral hygiene
- Poor nutritional status
- Insufficient oral care during treatment
- Exposure to oral stressors including alcohol and smoking
- Deranged renal and/or hepatic function
- Radiation therapy: dose, schedule and type like conformal or IMRT or conventional

# Pathogenesis

- Not fully elucidated.
- Recent advances in molecular and cell biology and translational research suggest, OM, a complex, *multistep process*.

- I. Initiation
- II. Message generation
- III. Signaling and amplification
- IV. Ulceration and inflammation
- V. Healing



RT induced OM typically appears toward the end of the **2<sup>nd</sup> week** of treatment, plateaus during the **4<sup>th</sup> week** of RT, and may persist for **2 to 3 weeks** once treatment is over.

# ASSESSMENT AND DOCUMENTATION

The oral cavity should be assessed regularly using *valid and reliable instruments* to document “normal pattern” of changes during the treatment

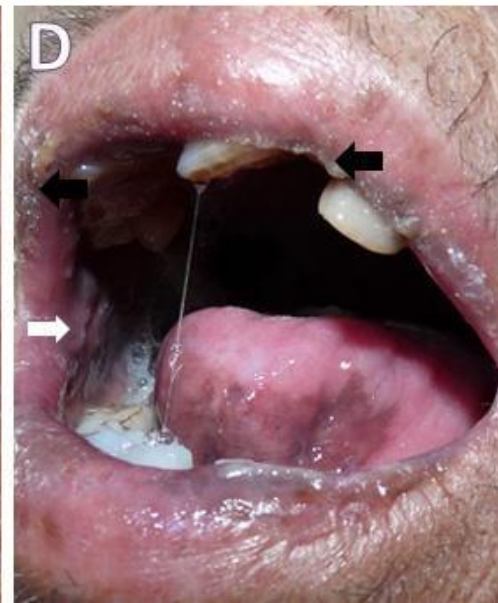
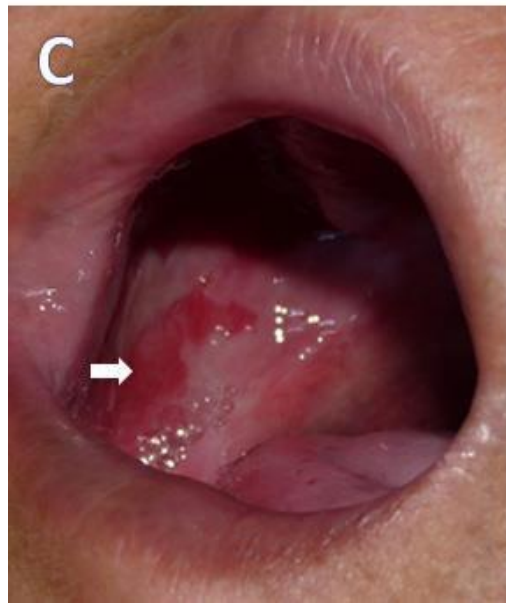
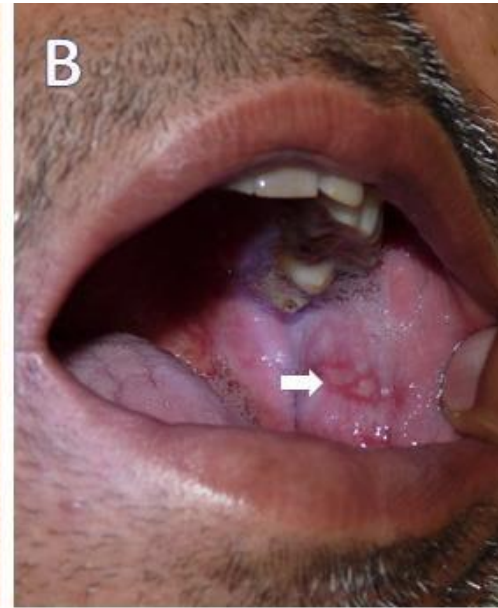
	<b>Grade 0</b>	<b>Grade 1</b>	<b>Grade 2</b>	<b>Grade 3</b>	<b>Grade 4</b>
<b>WHO<sup>1</sup></b>	None	Soreness with erythema	Erythema, ulcers, can <b>eat</b> solids	Ulcers, <b>liquid diet</b> only	Alimentation not possible
<b>RTOG<sup>2</sup></b>	No change over baseline	Irritation/ may experience mild <b>pain</b> not requiring analgesic	Patchy mucositis which may produce an inflammatory serosanguinitis discharge/ may experience <b>moderate pain</b> requiring analgesia	Confluent fibrinous mucositis/ may include <b>severe pain</b> requiring narcotic	Ulceration, hemorrhage or necrosis
<b>NCI-CTCAE v5.0<sup>3</sup></b>	None	Asymptomatic or mild symptoms; intervention not indicated	<b>Moderate pain</b> ; not interfering with oral intake; <b>modified diet</b> indicated	<b>Severe pain</b> ; interfering with <b>oral intake</b>	Life-threatening consequences; <b>urgent intervention</b> indicated.

*WHO: World Health Organization,*

*RTOG: Radiation therapy oncology group,*

*NCI-CTCAE: National Cancer Institute Common Toxicity Criteria for Adverse Events*

1. World Health Organization. (1979) *WHO Handbook For Reporting Results Of Cancer Treatment*. Geneva, Switzerland: World Health Organization. 15-22.
2. Cox JD, Stetz J, Pajak TF. (1995) *Toxicity criteria of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC)*. *Int J Radiat Oncol Biol Phys*. 31:1341-1346.
3. *Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0 Published: November 27, 2017*



# **Intervention to reduce toxicity and to increase compliance**

- Before starting the treatment
- After start of the treatment

# Before starting the treatment

- Counselling
- During radiotherapy planning
  - Techniques:  
2D vs. 3D vs. IMRT



# Counselling



- ✓ OM typically appears toward the end of the 2<sup>nd</sup> week
- ✓ Plateaus during the 4<sup>th</sup> week of Radiotherapy
- ✓ May persist for 2 to 3 weeks once treatment is over



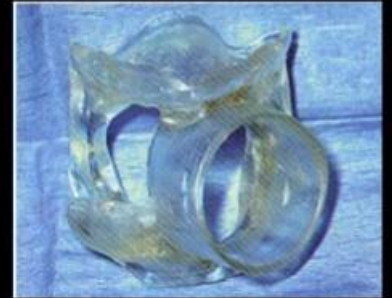
- During radiotherapy planning
  - 2D – blocks, displacement
  - 3D- blocks, unilateral
  - IMRT
  - Delineation of Oral Mucosa

# Techniques: 2D

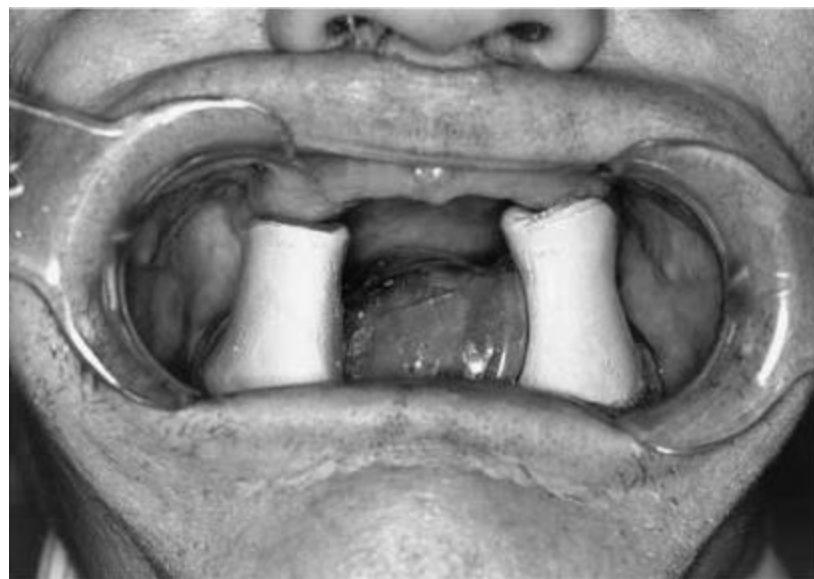
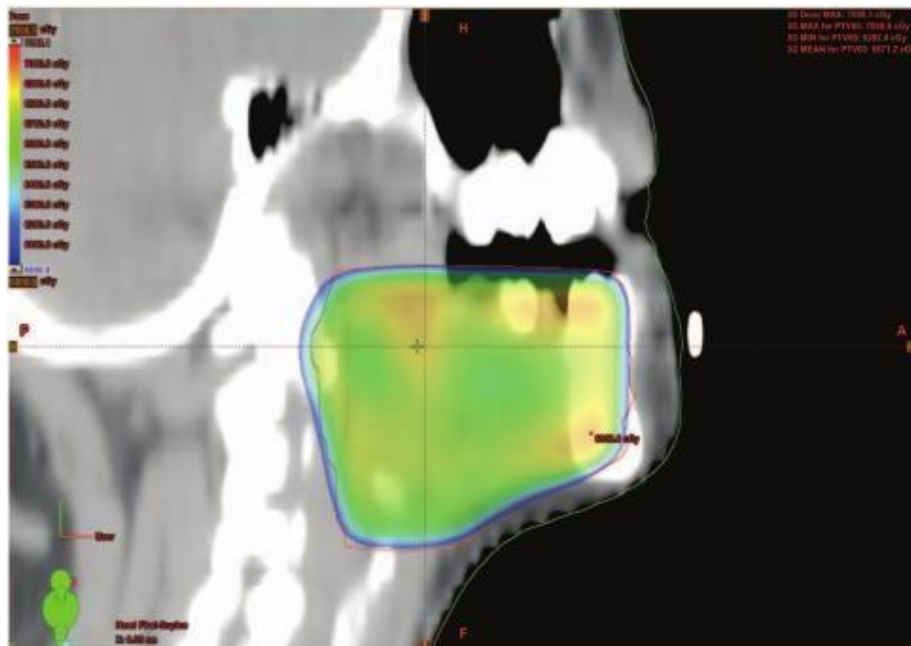
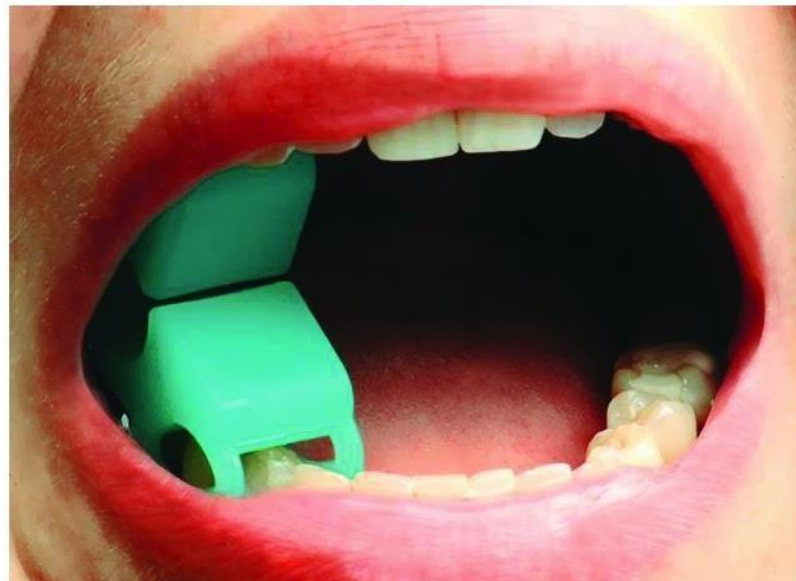
- Displacement techniques
  - Intra-oral stents
  - Bite blocks
  - ? ‘Stuck out tongue’



- ▣ Removing structures from the radiation field
- ▣ Positioning peroral cones

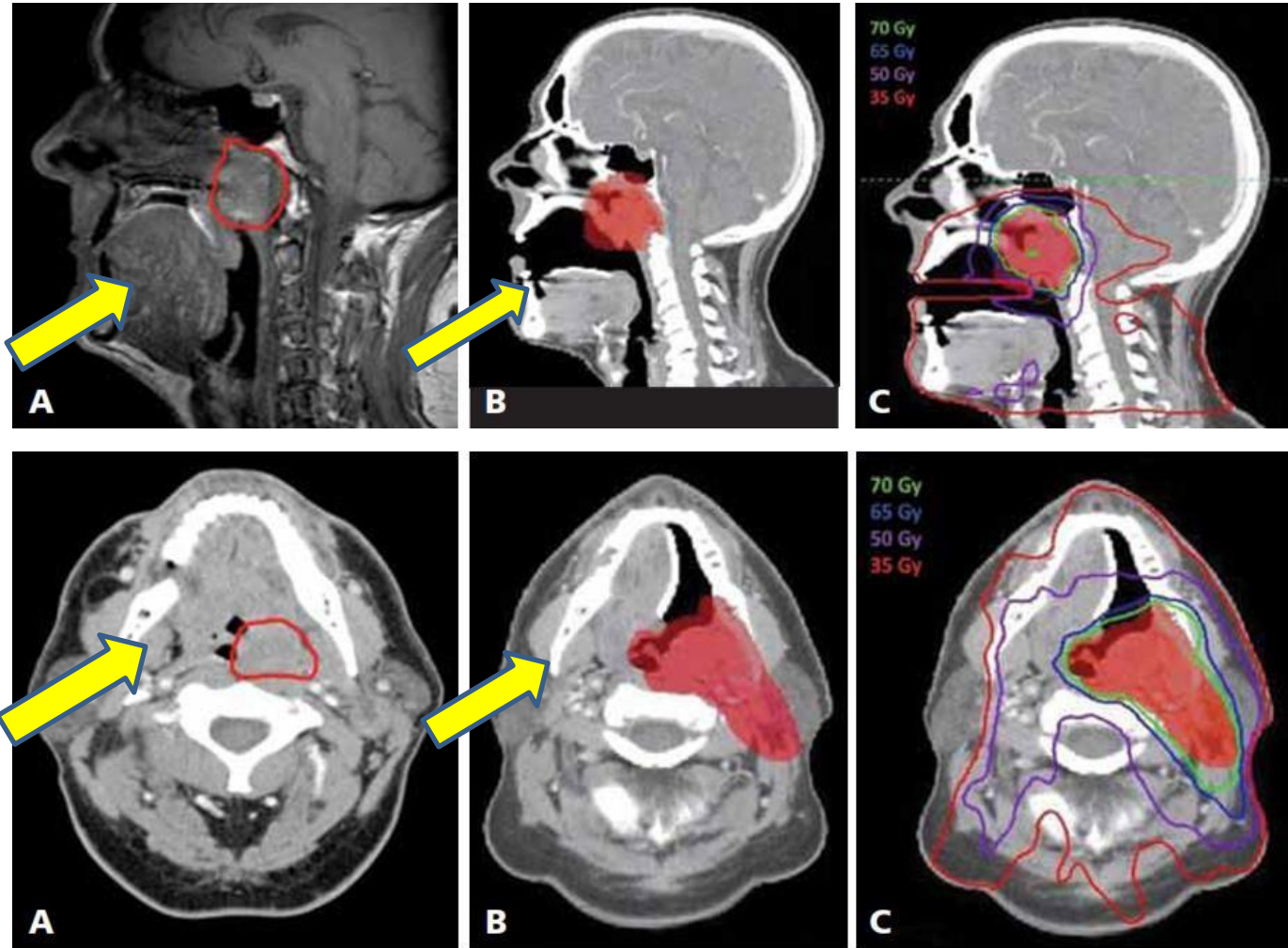
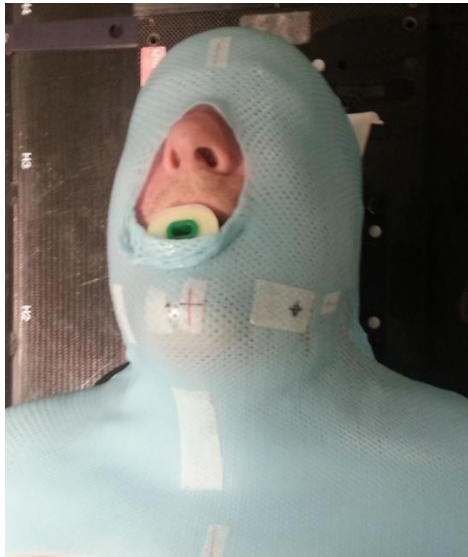


# Tongue displacement devices



# Techniques: 3D conformal

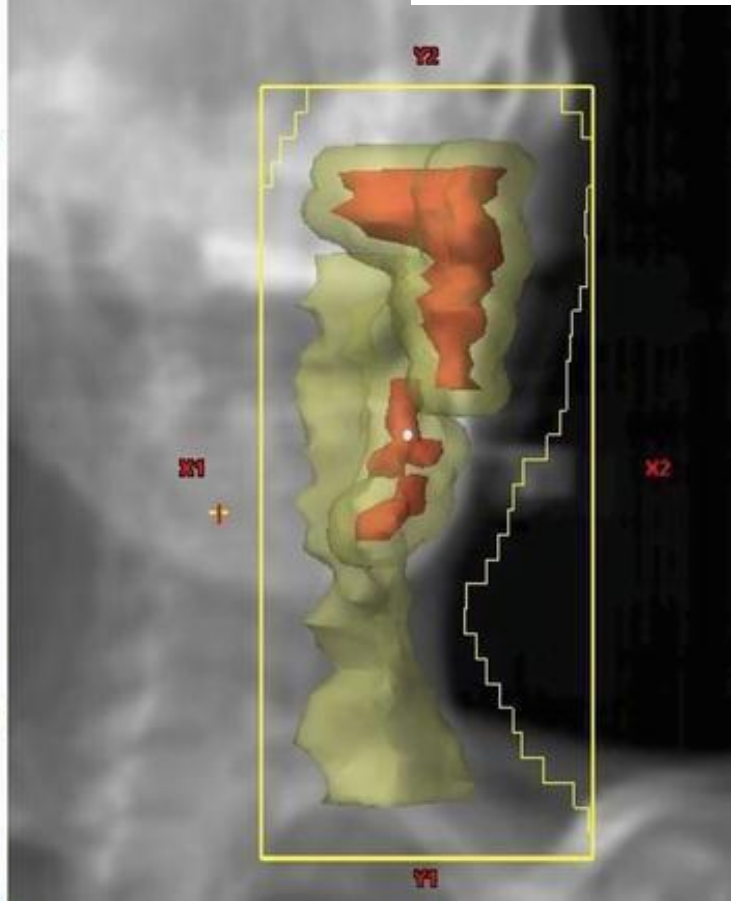
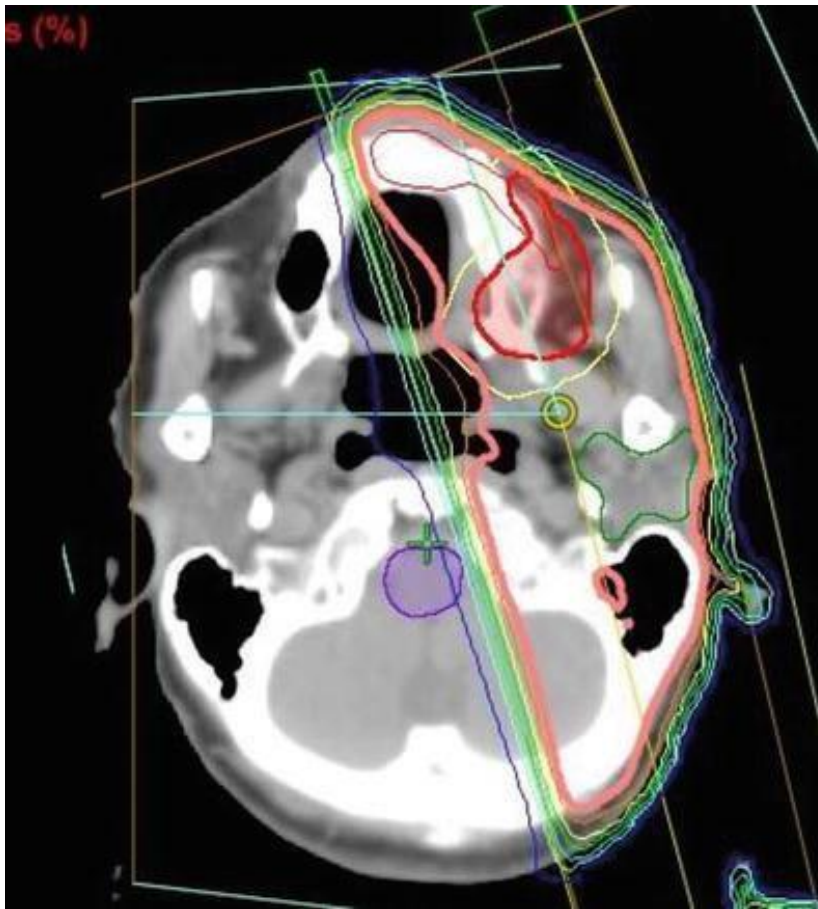
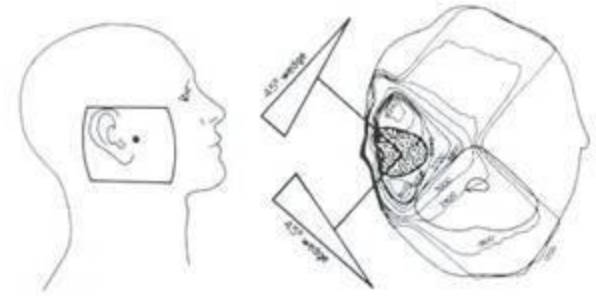
Refine volume of irradiation by displacement techniques





# Techniques: 3D conformal

Ipsilateral irradiation in selected cases



# Comparison of 3D Conformal Radiotherapy and Intensity Modulated Radiotherapy with or without Simultaneous Integrated Boost during Concurrent Chemoradiation for Locally Advanced Head and Neck Cancer

April 2014 | Volume 9 | Issue 4 | e94456

Category	Indicator	3D-CRT <sup>1</sup> (n = 125)	IMRTseq <sup>2</sup> (n = 120)	IMRT+SIB <sup>3</sup> (n = 134)	<i>P</i> value
Feeding tube during RT <sup>4</sup>	Yes	100 (80.0%)	61 (50.8%)	59 (44.0%)	<.0001
	No	25 (20.0%)	59 (49.2%)	75 (56.0%)	
Greater than 10% weight loss during RT	Yes	48 (38.4%)	64 (53.3%)	70 (52.2%)	.10
	No	38 (30.4%)	26 (21.7%)	43 (32.1%)	
	N.S. stated	39 (31.2%)	30 (25.0%)	30 (22.4%)	
Grade $\geq 3$ mucositis	Yes	55 (44.0%)	44 (36.7%)	30 (22.4%)	<.0001
	No	48 (38.4%)	54 (45.0%)	91 (67.9%)	

Although all the RT techniques results in the varying grades of OM but with the help of IMRT we can spare the mucosa and thus limit the acute and long term morbidity associated with grade 3 and 4 OM



Contents lists available at [ScienceDirect](http://www.sciencedirect.com)

# Radiotherapy and Oncology

journal homepage: [www.thegreenjournal.com](http://www.thegreenjournal.com)

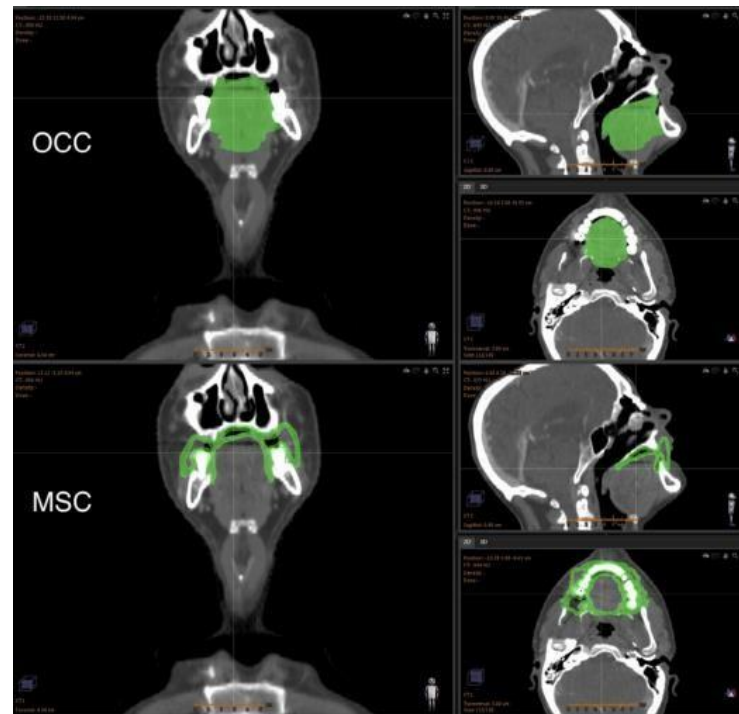


Delination of oral mucosa

## A novel method for delineation of oral mucosa for radiotherapy dose–response studies



Jamie A. Dean <sup>a,\*</sup>, Liam C. Welsh <sup>b</sup>, Sarah L. Gulliford <sup>a</sup>, Kevin J. Harrington <sup>b</sup>, Christopher M. Nutting <sup>b</sup>





Contents lists available at [ScienceDirect](#)

# Radiotherapy and Oncology

journal homepage: [www.thegreenjournal.com](http://www.thegreenjournal.com)

Deliniation of oral mucosa

## A novel method for delineation of oral mucosa for radiotherapy dose–response studies



Jamie A. Dean <sup>a,\*</sup>, Liam C. Welsh <sup>b</sup>, Sarah L. Gulliford <sup>a</sup>, Kevin J. Harrington <sup>b</sup>, Christopher M. Nutting <sup>b</sup>

<sup>a</sup>Joint Department of Physics at The Institute of Cancer Research and The Royal Marsden NHS Foundation Trust; and <sup>b</sup>Head and Neck Unit, The Royal Marsden NHS Foundation Trust, London, UK

### A B S T R A C T



There is currently **no standard method for delineating the oral mucosa** and most attempts are oversimplified. A new method to obtain anatomically accurate contours of the oral mucosa surfaces was developed and applied to 11 patients. This is expected to represent an opportunity for improved toxicity modelling of oral mucositis.

© 2015 The Authors. Published by Elsevier Ireland Ltd. Radiotherapy and Oncology 115 (2015) 63–66

This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).





[Cureus](#). 2022 Mar; 14(3): e23716.

PMCID: PMC9056708

Published online 2022 Mar 31. doi: [10.7759/cureus.23716](https://doi.org/10.7759/cureus.23716)

PMID: [35505730](https://pubmed.ncbi.nlm.nih.gov/35505730/)

## Delineation of Oral Mucosa as a Pseudo-Organ-at-Risk May Lead to a Decrease in the Incidence of Oral Mucositis: A Dosimetric Analysis of Intensity-Modulated Radiation Therapy Plans in Head and Neck Cancers

Monitoring Editor: Alexander Muacevic and John R Adler

[Himanshi Khattar](#),<sup>1</sup> [Piyush Kumar](#),<sup>✉1</sup> and [Navitha S](#)<sup>1</sup>

➤ After start of the treatment

# Management of Oral Mucositis

Multinational Association of  
Supportive Care in Cancer

&

International Society for Oral  
Oncology

**(MASCC/ISOO)**

has advocated and updated time to  
time the guidelines  
for the prevention and treatment  
of CT- and RT-induced OM.



•Keefe DM, Schubert MM, Elting LS, Sonis ST, Epstein JB, Raber-Durlacher JE, Migliorati CA, McGuire DB, Hutchins RD, Peterson DE. (2007) Mucositis Study Section of the Multinational Association of Supportive Care in Cancer, International Society for Oral Oncology. Updated clinical practice guidelines for the prevention and treatment of mucositis. *Cancer Mar. 1;109(5):820-31.*

# Management of Mucositis secondary to cancer treatment

## The 2019/20 MASCC/ISOO Clinical Practice Guidelines

Developed by the Mucositis Study Group

# Basic Oral Care (BOC) <sup>1/7</sup>

Intervention: **Professional oral care**

	LoE	Guideline category	Guideline
1	III	NGP / Expert opinion	<ul style="list-style-type: none"> <li>No guideline was possible regarding the use of <u>professional oral care</u> for the prevention of OM for patients with hematologic, solid or H&amp;N cancers due to limited and inconsistent data.</li> <li>An expert opinion complements this guideline. <b>Although, there was insufficient evidence to support the use of professional oral care for OM prevention, the panel is of the opinion that dental evaluation and treatment as indicated prior to cancer therapy is desirable to reduce the patient's risk for local and systemic infections from odontogenic sources.</b></li> </ul>

# Basic Oral Care

Backbone of radiotherapy treatment in HNC.

The “*basic oral care*” typically includes:

- Meticulous pretreatment assessment.
- Evaluation by dental specialists to eliminate caries and existing gum disease.
- Identification and elimination of preexisting potential sources of infection.

*Basic oral care protocols* during RT involve:

- Brushing in a non traumatic fashion with a soft-bristle toothbrush which has to be replaced on regular basis.
- The use of daily dental fluoride prophylaxis as (brushing) gels, rinses.
- They induce fluoride incorporation into tooth enamel and dentin.
- They also reduce oral bacterial load.



# Basic Oral Care (BOC) <sup>6/7</sup>

Intervention: **Bland Mouth Rinses**

	LoE	Guideline category	Guideline
6	III	NGP / Expert opinion	<ul style="list-style-type: none"> <li>No guideline was possible regarding the use of <u>saline</u> or <u>sodium bicarbonate</u> rinses in the prevention or treatment of OM in patients undergoing cancer therapy due to limited data for each intervention.</li> <li>An expert opinion complements this guideline. <b>Despite the limited data available for both saline and sodium bicarbonate, the panel recognizes that these rinses are inert bland rinses that increase oral clearance which may be helpful for maintaining oral hygiene and improving patient comfort.</b></li> </ul>

# Foundations Of Care

**Saline Gargle:** This saline solution is made by adding  $\frac{1}{2}$  tablespoon salt to 1 liter water and solution can be administered at room or refrigerated temperatures, depending on patient preference.



✓ *This maintain oral moistness.*

✓ *Increase oral lubrication by acting directly as well as by stimulating salivary glands to increase salivary flow*

✓ *The patient should rinse several times as often as necessary to maintain oral comfort.*

**Sodium bicarbonate (baking soda)**  $\frac{1}{2}$  tablespoons can be added, if viscous saliva is present.



# Basic Oral Care (BOC) <sup>7/7</sup>

Intervention: **Chlorhexidine**

	LoE	Guideline category	Guideline
7	III	Suggestion against	<ul style="list-style-type: none"> <li>The panel <b>suggests</b> that <u>CHX</u> <b>not be used</b> in the <b>prevention</b> of OM in patients undergoing <b>H&amp;N RT</b>.</li> </ul>

Use of *chlorhexidine*, antiseptic mouthwash is **NOT** recommended because it is associated with increase in oral mucosal inflammation, general mouth discomfort, taste alteration and staining of teeth

# Anti-inflammatory (1-2/2)

Intervention: **Benzydamine**

LoE	Guideline category	Guideline
10I	Recommendation	<ul style="list-style-type: none"> <li>The panel <b>recommends</b> <u>benzydamine</u> mouthwash for the prevention of OM in patients with H&amp;N cancer receiving a <b>moderate dose RT</b> (&lt;50 Gy).</li> </ul>
11II	Suggestion	<ul style="list-style-type: none"> <li>The panel <b>suggests</b> the use of <u>benzydamine</u> mouthwash for the prevention of OM in patients with H&amp;N cancer receiving <b>radio-chemotherapy</b>.</li> </ul>

***Benzydamine hydrochloride (BZD)*** is a nonsteroidal agent, exhibits, antimicrobial, anti-inflammatory, anesthetic, and analgesic effects.

Use of BZD was associated with significantly reduced erythema and ulceration and delays the need of systemic analgesics.

doi: 10.1007/s00520-016-3548-9. Epub 2016 Dec 16.

# Role of benzydamine hydrochloride in the prevention of oral mucositis in head and neck cancer patients treated with radiotherapy (>50 Gy) with or without chemotherapy

Madhup Rastogi<sup>1</sup>, Rohini Khurana<sup>2</sup>, Swaroop Revannasiddaiah<sup>3</sup>, Isha Jaiswal<sup>2</sup>, Sambit S Nanda<sup>4</sup>, Pooja Gupta<sup>5</sup>, Kundan S Chufal<sup>6</sup>, M L Bhatt<sup>7</sup>

Affiliations [+](#) expand

PMID: 27987094 DOI: 10.1007/s00520-016-3548-9

**Conclusion:** Benzydamine significantly reduces OM even at doses >50 Gy in HNC patients. Its role in patients receiving concurrent chemotherapy further needs to be evaluated.

# Natural remedies & Misc. (1-2/2)

vitamins, minerals and nutritional supplements

Intervention: **Glutamine**

	LoE	Guideline category	Guideline
12	I		
13	II	Suggestion	<p><b>H&amp;N</b>.</p> <ul style="list-style-type: none"> <li>The panel <b>suggests</b> <u>glutamine (per os)</u> for the prevention of OM in patients with <b>H&amp;N</b> cancer receiving <b>radio-chemotherapy</b>.</li> <li>The suggestion is with caution due to the higher mortality rate seen in HSCT patients treated with parenteral glutamine.</li> </ul>

# *Glutamine*

- Is a nonessential amino acid which reduces mucosal injury by reducing the production of proinflammatory cytokines and cytokines related apoptosis.
- Many malignancies are characterized by decreased glutamine levels.
- Glutamine supplementation can reverse this effect and may help to protect mucosal tissues from damage by RT or CT and thus accelerate recovery.
- Data suggest that this agent may be useful in preventing or reducing the incidence and severity of OM in patients undergoing cancer therapy
- Initially it was not recommended but now suggested.



# Natural remedies & Misc. (1/2)

Intervention: **Honey**

LoE	Guideline category	Guideline
14 II	Suggestion	<u>Honey</u> is <b>suggested</b> for the prevention of OM in <b>H&amp;N</b> cancer patients treated with either <b>RT or RT-CT</b> .

- Honey is a natural product that has been reported to have the best tissue healing properties.
- It has a *powerful impact on the proliferation* of B-lymphocytes and T-lymphocytes and also in the activation of macrophages.
- It *inhibits inflammatory process* by inhibiting cyclooxygenase pathway because it is the main pathway of inflammation.
- It *stimulates the process of granulation tissue*, angiogenesis, rapid epithelization and proliferation of fibroblasts.

# Antimicrobials, coating agents, anesthetics, analgesics (1-3/4)

Intervention: **Sucralfate**

LoE	Guideline category	Guideline
16	II Recommendation against	<u>Sucralfate</u> (combined topical and systemic) is <b>not</b> recommended for the <b>prevention</b> of OM-associated <b>pain</b> in <b>H&amp;N</b> cancer patients treated with <b>RT</b> .
17	II Recommendation against	<u>Sucralfate</u> (combined topical and systemic) is <b>not</b> recommended for the <b>treatment</b> of OM-associated <b>pain</b> in <b>H&amp;N</b> cancer patients treated with <b>RT</b> .
18	II Recommendation against	<u>Sucralfate</u> (combined topical and systemic) is <b>not</b> recommended for the <b>treatment</b> of OM-associated <b>pain</b> in solid cancer patients treated with <b>CT</b> .

# Antimicrobials, coating agents, anesthetics, analgesics (4/4)

Intervention: **Morphine**

	LoE	Guideline category	Guideline
19	III	Suggestion	<u>Topical morphine</u> 0.2% mouthwash is <b>suggested</b> for the treatment of OM-associated <b>pain</b> in <b>H&amp;N</b> cancer patients treated with <b>RT-CT</b> .



# Cryotherapy (2/2)

LoE	Guideline category	Guideline
21 II	Recommendation	The panel <b>recommends</b> using 30 minutes of oral <u>cryotherapy</u> to prevent oral mucositis in patients receiving <b>bolus 5-FU chemotherapy</b> during its infusion.

**Cryotherapy:** Use of ice chips.

- Causes cooling and local vasoconstriction and hence reduces blood flow to the oral mucosa.
- This reduces blood flow will also reduce the amount of drug reaching the oral mucous membranes, and may therefore reduce OM caused by CT drugs.
- The use of Cryotherapy is a readily available, cheap and effective method of minimizing OM with chemotherapy.

# PBM (Laser/light) therapy (2/3)

LoE	Guideline category	Guideline
25	II	<p>Recommendation</p> <ul style="list-style-type: none"> <li>The panel <b>recommends the use of intra-oral PBM therapy</b> using low level laser therapy for prevention of OM in adult patients receiving <b>RT to the H&amp;N (without CT)</b> (Table); following the specific PTPs of the selected protocol is recommended for optimal therapy.</li> <li>Safety considerations unique to patients with oral cancer should be considered.</li> </ul>

## Photobiomodulation therapy

Protocol	Wave-length (nm)	Power density (irradiance; mW/cm <sup>2</sup> )	Time per spot (sec)	Energy density (fluence; J/cm <sup>2</sup> )	Spot size (cm <sup>2</sup> )	Number of sites	Distance from the tissue	Frequency	Duration
#1	632.8	24	125	3.0	1	12	<1 cm	5 days / wk	Entire RT course

**Low-level laser therapy (LLLT)** or “soft laser” have analgesic, anti-inflammatory, and wound healing effects by speeding up the oral re-epithelialization.

There is no known clinical toxicity or side effects of the application of low-energy helium-neon lasers (soft lasers) and it positively influence the outcome of OM.



## Photobiomodulation Therapy in Oral Mucositis and Potentially Malignant Oral Lesions: A Therapy Towards the Future

[Reem Hanna](#),<sup>1,2,\*</sup> [Snehal Dalvi](#),<sup>1,3</sup> [Stefano Benedicenti](#),<sup>1</sup> [Andrea Amaroli](#),<sup>4</sup> [Tudor Sălăgean](#),<sup>5</sup> [Ioana Delia Pop](#),<sup>5</sup> [Doina Todea](#),<sup>6</sup> and [Ioana Roxana Bordea](#)<sup>7</sup>

- Low level laser therapy represents more than a promising agent to prevent or treat cancer—therapy induced OM.
- With diode and new technologies, laser is now less time-consuming and extraoral applicators with specific wavelength could be helpful to treat other sites of mucositis and skin toxicities.
- Also it may be used by trained paramedical staff like nurses who can complete clinician contribution.

# Pain management

- Pain is the single most important distressing symptom.
- Pain can also leads to decreased oral intake leading to malnutrition and the need for total parenteral nutrition (TPN).
- Most patients require both *systemic and topical analgesics*.
- Many local anesthetics agents, such as viscous xylocaine, lidocaine as oral solutions, are frequently used for the temporary relief of OM related pain.
- However such topical anesthetic interfere with taste perception, thus possibly contributing to hypo alimentation.
- *Narcotic analgesics* in the form of morphine, transdermal fentanyl patches along with laxatives can be administered. The dose of narcotic analgesic, their frequency, and duration should be regularly adjusted to meet the intensity level of pain.

# Targeting infection

- ✓ The oral cavity harbors a variety of pathogenic microorganisms, however healthy individuals are not susceptible to infection due to maintained mucosal integrity and normal immunity.
- ✓ But in cancer patients, already immunocompromised and due to loss of mucosal integrity, oral infections can arise from viral, fungal, and bacterial sources.
- ✓ Many authors have emphasized the necessity of a variety of *disinfectant, antibacterial, antiviral, and antifungal* agents for the *prophylaxis* and treatment of OM, but due to variable results, there is no uniform consensus and therefore, **Routine use is not recommended.**
- ✓ Keeping a high index of suspicion, culture and sensitivity should be done if infection is anticipated.

**Hydrogen peroxide rinses:** Daily use is **NOT** recommended because of the potential for damage to fibroblasts and keratinocytes, which can cause delayed wound healing.

✓ Using 3% hydrogen peroxide diluted 1:1 with water or normal saline to remove hemorrhagic debris may be helpful for **1 to 2 days**.

**Magic mouthwash or Mouthwash cocktail:** is used by different institutions across the world with a variety of ingredients like lidocaine, diphenhydramine, topical antifungal nystatin and an antacid containing aluminum/magnesium hydroxide in equal parts.

✓ These formulae are popular for OM treatment owing to its pain-relieving properties and its coating of the mucosa. MASCC/ISOO guidelines do not recommends use of such cocktail mouth wash for the prevention and treatment of OM.



# Radiation dermatitis

- During radiation therapy, the first few fractions causes immediate structural tissue damage.
- The destruction of a large proportion of basal keratinocytes results in the disruption of the self-renewing property of the epidermis.
- Repeated exposures do not allow time for basal skin cells to replenish and maintain optimal renewal of the epidermis.
- During a fractionated course of 2 Gy per fraction of radiation therapy, erythema occurs at doses of 12 to 20 Gy, dry desquamation occurs at doses  $\geq 20$  Gy, and moist desquamation occurs at doses  $> 50$  Gy or higher

# RTOG

RTOG ACUTE Radiation Morbidity				
Tissue	Grade 1	2	3	4
Skin	Follicular, faint or dull erythema / epilation / <i>dry desquamation</i> / decreased sweating	Tender or bright erythema, <i>patchy moist desquamation</i> / moderate edema	<i>Confluent</i> , moist desquamation other than skin folds, pitting edema	Ulceration, haemorrhage, necrosis

# CTCAE v5

CTCAE v5	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
<b>Dermatitis radiation</b>	<b>Faint erythema or dry desquamation</b>	<b>Moderate to brisk erythema; patchy moist desquamation, mostly confined to skin folds and creases; moderate edema</b>	<b>Moist desquamation in areas other than skin folds and creases; bleeding induced by minor trauma or abrasion</b>	<b>Life-threatening consequences; skin necrosis or ulceration of full thickness dermis; spontaneous bleeding from involved site; skin graft indicated</b>	<b>Death</b>

# General skin care

General skin care measures for patients undergoing radiation therapy include:

- Keeping the irradiated area clean and dry.
- Washing with lukewarm water and mild soap (liquid, synthetic, "soap-free" and fragrance-free body washes with a near-physiologic pH of 4 to 6 are preferable).
- Using unscented, lanolin-free, water-based moisturizers two to three times per day, including a nontreatment day on the weekend.
- Avoiding skin irritants, such as perfumes and alcohol-based lotions.
- Wearing loose-fitting clothes to avoid friction injuries.
- Avoiding corn starch or baby powder in skin folds.
- Avoiding sun exposure.
- Avoiding wet shaving within the treatment area; an electric razor is a safe alternative.

# Washing

- The benefit of a washing during treatment has been evaluated in a few randomized trials in head and neck cancer and in one meta-analysis.
- Although washing practices do not seem to reduce the overall risk of developing radiation dermatitis, washing with soap and water or water alone is associated with a significant reduction in itching, erythema, and desquamation compared with no washing.
- Moreover, allowing patients to continue their normal hygiene routine may prevent unnecessary distress and social isolation.

## Topical corticosteroids

- Use of topical corticosteroids are recommended for the prevention of severe radiation dermatitis and for the reduction of discomfort and itching.
- Low- to medium-potency topical corticosteroids, such as mometasone furoate 0.1% or hydrocortisone butyrate 0.1% cream, are applied to the treatment field once or twice daily, starting on the day of the first radiotherapy session and continued through the entire treatment cycle.

## Other agents

Evidence from a limited number of randomized trials does support

- ✓ Silicone-based gel dressings
- ✓ Silver nylon dressings
- ✓ Silver sulfadiazine

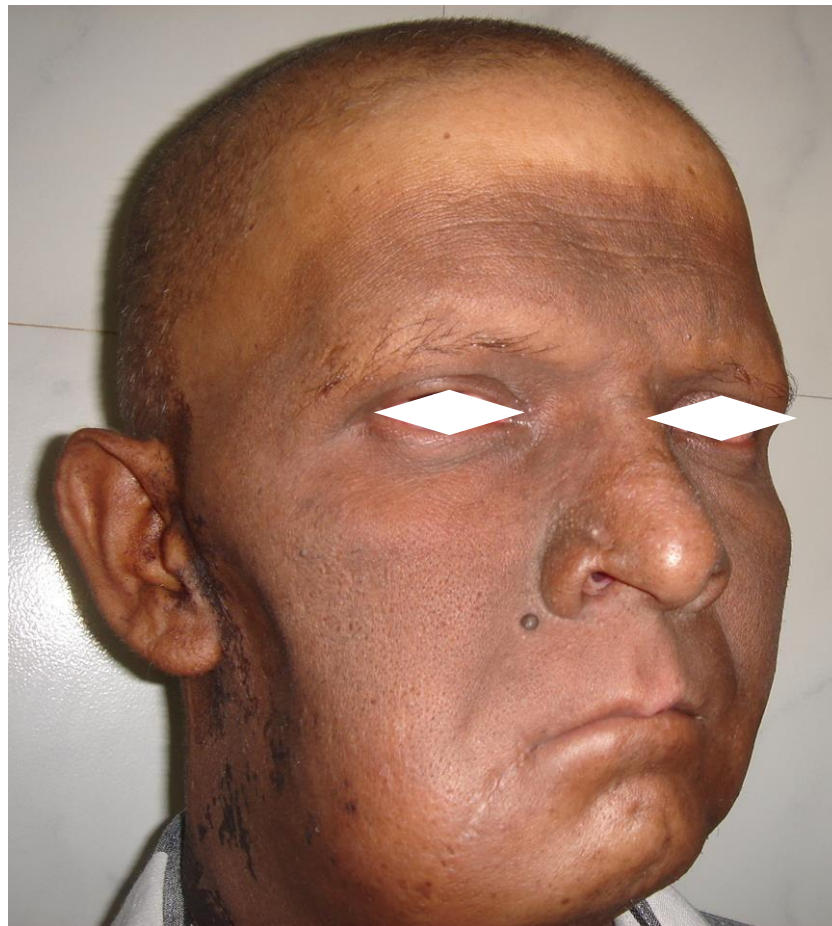
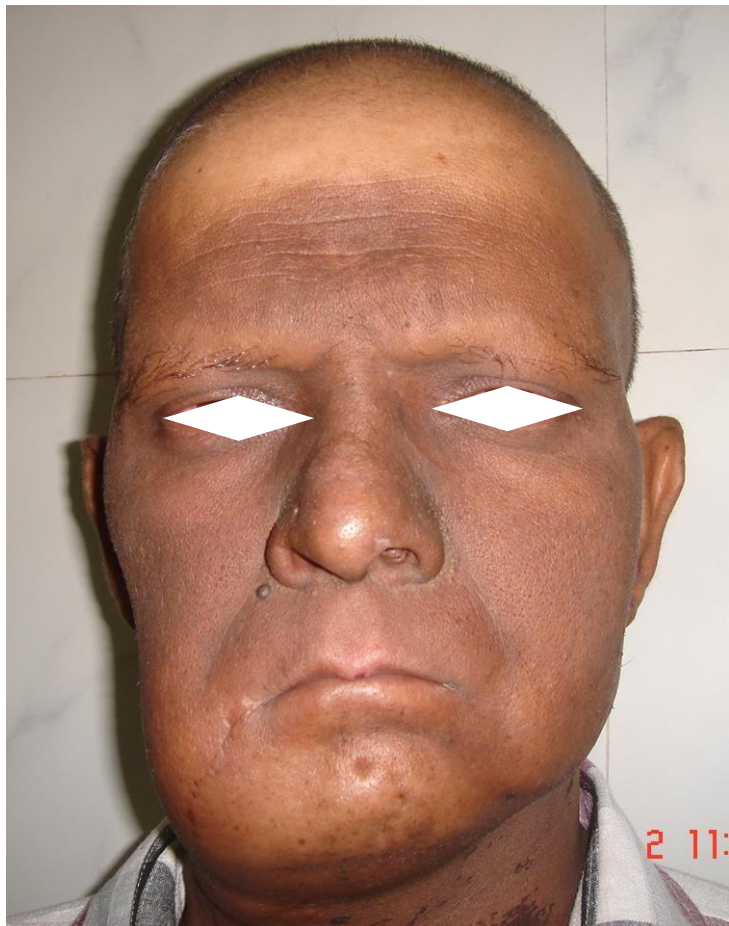
## *Commercially available Soothing and Moisturizing Lotion for radiation dermatitis*

**Ingredients:** DL water, Calandula, Prunus Amygdalus Oil (Almond), Aloe Vera, Simmondsia, Jojoba, Glycerin, Light Liquid Parafin, Isopropyl Myristate, Bees Wax, Emulsifying Wax, Glycerol Monostearate, Tocophryl (Vitamin E), Allantoin, Phenoxy Ethanol, Methyl Paraben, Propyl Paraben, Mentha Piperita, Dimethicone.

**Ingredients:** Purified Water, Cetostearyl Alcohol, Coconut Oil, Caprylic/Capric Triglyceride, Isopropyl Myristate, Glycerin, Glyceryl Stearate (and) PEG-100 Stearate, Bees Wax, Alkyl Ester, Glyceryl Monostearate, Calendula Oil, Pentavitin (Saccharide Isomerate (and) Aqua (and) Citric Acid (and) Sodium Citrate), Sweet Almond Oil, Aloe vera Extract, Betaine, Niacinamide, Shea Butter, Sodium PCA, Sodium Benzoate, Imid Urea, Potassium Sorbate, Allantoin, Citric Acid, Vitamin E, Lavender oil, Sodium Gluconate & Carbomer.



# Caution



# Dysphagia

- Dysphagia (difficulty swallowing) is a common side effect of head and neck cancer.
- Dysphagia can make it difficult or painful to eat and drink, and can lead to malnutrition, dehydration, and weight loss.
- It tends to worsen throughout treatment once it occurs, and in severe cases, can lead to cachexia muscle wasting, anorexia, and anemia.

## RTOG ACUTE Radiation Morbidity

Tissue	Grade 1	2	3	4
Pharynx & esophagus	<i>Mild</i> dysphagia or odynophagia / may require topical anesthetic or <i>non-narcotic analgesics</i> / may require <i>soft diet</i>	<i>Moderate</i> dysphagia or odynophagia / may require <i>narcotic analgesics</i> / may require puree or <i>liquid diet</i>	<i>Severe dysphagia</i> or odynophagia with dehydration or weight loss > 15% from pretreatment baseline requiring <i>NG feeding tube, IV fluids</i> , or hyperalimentation	Complete obstruction, ulceration, perforation, fistula

## CTCAE v5



Tissue	Grade 1	2	3	4
Dysphagia	Symptomatic, able to eat regular diet	Symptomatic and altered eating/swallowing	Severely altered eating/swallowing; tube feeding, TPN, or hospitalization indicated	Life-threatening consequence; urgent intervention indicated

# Dysphagia: Management

The cancer care teams should not wait for symptoms to appear to address dysphagia. Prophylactic interventions to reduce the risk of radiation dysphagia are as follows:-

- Dietary counselling
- Use of local anaesthetics
- Anti-inflammatory and pain medication
- Naso gastric tube placement
- PEG tube placement
- Dysphagia-optimized IMRT (DO-IMRT) minimize radiation dose to swallowing-involved musculature and nerves to reduce dysphagia risk.
- Swallowing exercises: PMR

## Dysphagia-optimised intensity-modulated radiotherapy versus standard intensity-modulated radiotherapy in patients with head and neck cancer (DARS): a phase 3, multicentre, randomised, controlled trial

[Prof Christopher Nutting, FRCR](#)   • [Laura Finneran, MSc](#) • [Justin Roe, PhD](#) • [Mark A Sydenham, BSc Hons](#) • [Matthew Beasley, FRCR](#) • [Shree Bhide, FRCR](#) • et al. [Show all authors](#)

[Open Access](#) • Published: July 06, 2023 • DOI: [https://doi.org/10.1016/S1470-2045\(23\)00265-6](https://doi.org/10.1016/S1470-2045(23)00265-6)

### **Interpretation:**

Our findings suggest that DO-IMRT improves patient-reported swallowing function compared with standard IMRT. DO-IMRT should be considered a new standard of care for patients receiving radiotherapy for pharyngeal cancers.



# Toxicities and clinical outcome of adjuvant dysphagia optimized versus standard intensity-modulated radiotherapy for post-operative oral cavity cancers: A prospective comparative study

Ayushi Patni <sup>1</sup>, [Madhup Rastogi](#) <sup>1</sup>, Ajeet Kumar Gandhi <sup>1</sup>, Vachaspati Kumar Mishra <sup>1</sup>, Anoop Kumar Srivastava <sup>1</sup>, Vikas Sharma <sup>2</sup>, Akash Agarwal <sup>2</sup>, Rohini Khurana <sup>1</sup>, Rahat Hadi <sup>1</sup>, Shantanu Sapru <sup>1</sup>, Surendra Prasad Mishra <sup>1</sup>

Affiliations [+](#) expand

PMID: 37814926 DOI: [10.1002/hed.27541](#)

**Conclusion:** DARS (dysphagia aspiration-related structures) can be spared in PO-OCSCC patients treated with Do-IMRT without compromising coverage of the target volumes. Limiting doses to DARS leads to lesser acute and late toxicity without compromising locoregional control.

*The DARS include superior, middle, and inferior pharyngeal constrictor muscles, glottis, and supraglottic larynx, base of the tongue, and upper esophageal sphincter including cricopharyngeus muscle and upper esophagus.*



# Xerostomia (*early & late*)

- Xerostomia, also known as dry mouth
- It is caused when the salivary glands do not produce enough saliva to keep the mouth moist.
- Salivary function is extremely sensitive to irradiation.
- Acute changes involves the decreased water content due to involvement of acinar system and later on damages the duct system also.

## *Symptoms includes:*

- *Dry, sticky feeling in the mouth*
- *Saliva that is thick or stringy*
- *Painful, burning sensation in the mouth or tongue*
- *Difficulty chewing or swallowing*
- *Change in taste*
- *Difficulty talking*

**In addition to the physical discomfort, dry mouth can interfere with both the dental health and ability to eat (leading to infection and/or malnutrition).**

# Intervention for Xerostomia

## Prevention



- Spare salivary glands as much as feasible by meticulous planning
- IMRT is standard of care (PARSPORT trial)
- Maintenance of excellent oral hygiene & frequent water intake
- Radioprotective agents: Amifostine (not in routine clinical use any more)
- Salivary gland relocation

## Symptomatic management

- Daily living tricks like water bottle. Stay hydrated.
- Saliva substitutes and mouth rinses or artificial saliva.
  - ✓ Water, Glycerin, Sorbitol, Propylene Glycol, carbo methyl cellulose
- Sugar-free chewing gum/ candy or mouth dissolving Xylitol tablets to stimulate the salivary glands.
- Pilocarpine or cevimeline which stimulate the salivary glands.

*This information is based on the joint ISOO/MASCC/ASCO guideline*

## Parotid-sparing intensity modulated versus conventional radiotherapy in head and neck cancer (PARSPORT): a phase 3 multicentre randomised controlled trial

Dr Christopher M Nutting, FRCR   • James P Morden, MSc • Kevin J Harrington, FRCR •

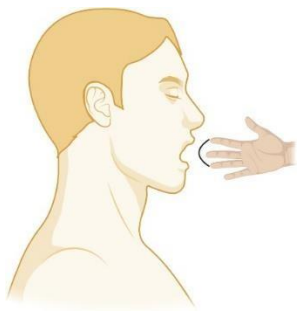
Teresa Guerrero Urbano, PhD • Shreerang A Bhide, FRCR • Catharine Clark, PhD • et al. [Show all authors](#) •

[Show footnotes](#)

[Open Access](#) • Published: January 13, 2011 • DOI: [https://doi.org/10.1016/S1470-2045\(10\)70290-4](https://doi.org/10.1016/S1470-2045(10)70290-4)

### Interpretation

Sparing the parotid glands with IMRT significantly reduces the incidence of **xerostomia** and leads to recovery of saliva secretion and improvements in associated quality of life, and thus strongly supports a role for IMRT in squamous-cell carcinoma of the head and neck.



# Trismus



- Normal mouth opening varies within the range of 45 – 50 mm
- Inability to open mouth is trismus.
- Common morbidity associated with head and neck cancer radiotherapy
- Aggravated due to pre existing SMF, muscle involvement, post surgical patients.
- Higher the radiation doses delivered to the masticatory structure, the worse is the restriction in mouth opening
- Reirradiation due to recurrences are at higher risk than patients receiving their first treatment.
- Abnormal proliferation of fibroblast in the muscle and ligaments (radiation induced fibrosis)
- The reduction in mouth opening usually begins to appear at the end of radiation course and continues to deteriorates in the following year.

# Management of Trismus

## Physical therapy

- Start exercise during or soon after the completion of radiation therapy.
- Active exercise aim to strengthen the jaw opening muscles (depressors of the mandible).  
Passive exercise stretch the jaw-closing muscles (elevators of the mandible)
- Delaying the exercise, lowers the results and increase the trismus.

## Trismus Appliances

- Impart mechanical forces to forcibly stretch the jaw closing muscles by depressing the mandible.
- Patient may open the mouth actively (if possible) using their own jaw-opening muscles, the appliance is then inserted, and the number of spatulas are counted. This helps the patient to set goals and record progress.

## Drug Therapy

- Pentoxifylline + Vitamin E for at least 6 months

## Release Surgery

- Resection of scar tissue and fibrotic band along with reconstruction of surgical defects can alleviate some of the restriction and improve trismus.
- All release-reconstructive surgeries must be followed by strict physical therapy program
- Patients selected for these types of surgeries have to be cooperative and well motivated.





**TrisCaRe**  
MOUTH OPENING  
DEVICE

**iCanCaRe**  
*The Hospital Leader*  
Innovative Cancer Care and  
Rehabilitation Pvt Ltd

The packaging is a white rectangular box with a blue border. It features the TrisCaRe logo at the top, the product name in the middle, a circular inset image of a man using the device, and the iCanCaRe logo and company name at the bottom.



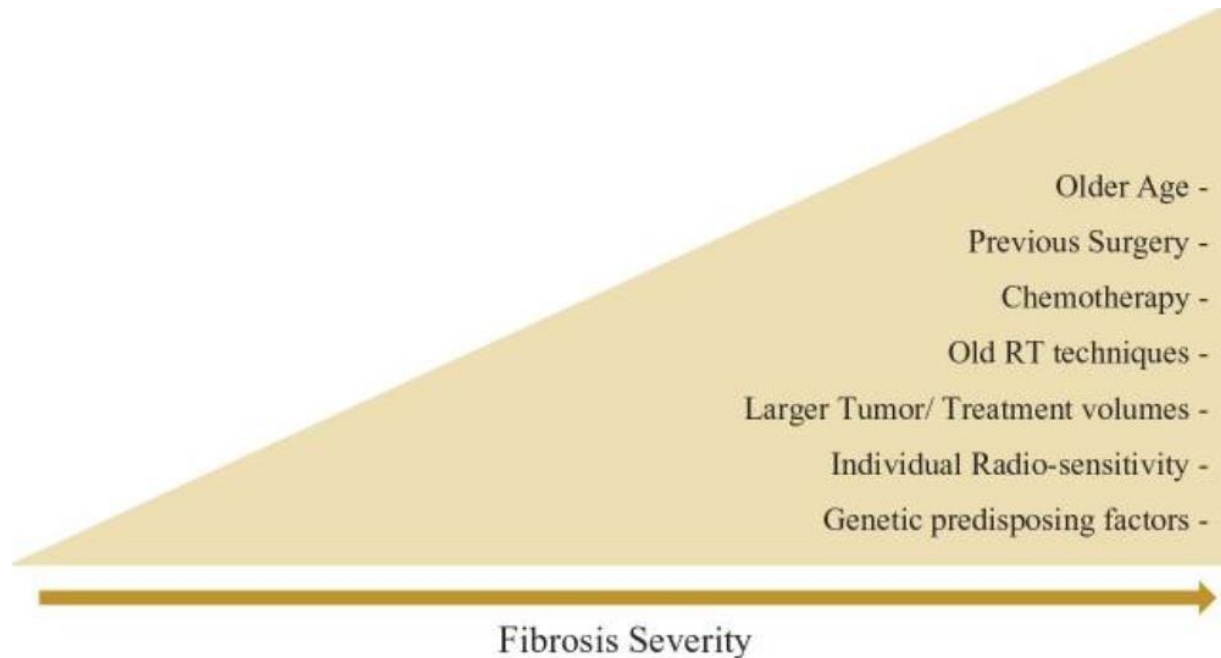
## Sub cutaneous fibrosis of neck

- Radiotherapy-related fibrosis remains one of the most challenging treatment related late side effect.
- This can be attributed to a chronic inflammatory process due to repetitive injury induced by RT.
- Due to the excess production of fibroblasts and dysregulation of the wound healing processes.
- This process can manifest as neck stiffness, trismus, and may be associated with lymphedema.



# CTCAE v5

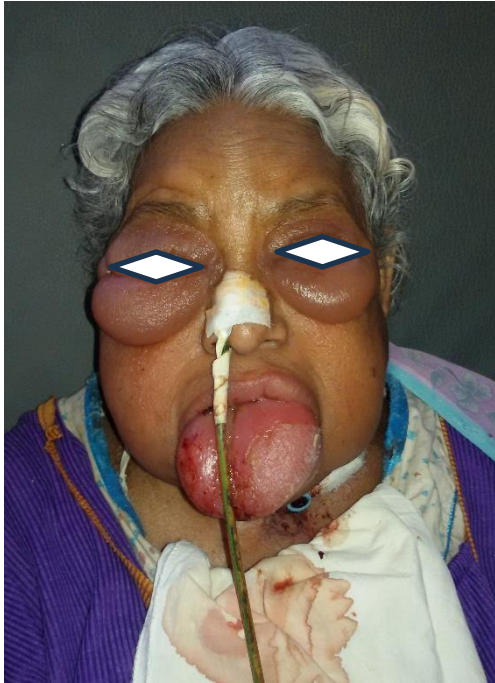
Tissue	Grade 1	2	3	4
Fibrosis deep connective tissue	<i>Mild</i> induration, <i>able to move</i> skin parallel to plane (sliding) and perpendicular to skin (pinching up)	<i>Moderate</i> induration, <i>able to slide skin</i> , unable to pinch skin; limiting instrumental ADL	<i>Severe</i> induration; <i>unable to slide</i> or pinch skin; limiting joint or orifice movement (e.g., mouth, anus); limiting self care ADL	Generalized; associated with signs or symptoms of <i>impaired breathing or feeding</i>



- The treatment approach consists of either systemic treatments, topical treatments, or mechanical treatments in addition to palliative measures.
- Mechanical maneuvers are often used preventatively.
- Pentoxifylline, a xanthine derivative, has been used off-label in combination with Vitamin E (tocopherol), a free radical scavenger, to treat of radiation-induced fibrosis.
- Pentoxifylline is involved in downregulating protein kinases and other inflammatory cytokines. It also inhibits intracellular signaling to TFG- $\beta$ , a pathway significantly involved in radiation fibrosis.
- Pentoxifylline, with and without tocopherol, displayed promising results in the treatment of fibrosis.

# Lymphedema

- Often coexists with neck fibrosis.
- When the lymphatic load exceeds the transport capacity of the lymphatic system secondary to tumor and/ or surgery and/or radiation
- Increased incidence in post operative cases and with bilateral neck dissection



## Intervention

- At the time of planning especially in high risk cases, sufficient margin in the nape of the neck to be given.
- Face, neck and oral cavity exercises
- Steroids
- Pentoxifylline + Vitamin E for at least 6 months

# Conclusion

- Pretreatment assessment and counseling: Gold standard.
- Honest and detailed communication.
- Weekly assessment, early diagnosis.
- Evidence based timely *intervention to reduce toxicity and to increase compliance.*

**Thank you**