DRUG LAB 2 – Terapia di supporto in corso di radio-chemioterapia radicale per tumori del distretto testa collo

Terapia topica cutanea e mucosa

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Radioterapia e Oncologia clinica

CONFLICT OF INTEREST

- I have no disclosures

DERMATITIS RADIATION

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- In spite of technological advancements (IMRT, skin-sparing techniques…) it remains a prominent adverse reaction that can negatively affect QoL, cause infection or sepsis, and lead to **treatment interruptions**.
- Currently, clinical management is highly variable due to lack of standardization in prevention/management of skin reactions

Prevention

- Inconsistent evidence:
  - Topical non-steroidal agents (Hyaluronic acid/Urea/Heparinoid/Trolamine)
  - Topical steroidal agents (hydrocortisone, beclomethasone)
  - Dressings (e.g. polyurethan, hydrofilm)
  - Topical natural agents (e.g. Curcumin, calendula, chamomilla, honey)
  - Deodorants (alluminium), water & soap

- Evidences:
  - Low-Level Laser Therapy (LLLT)
  - Topical steroid agents (**mometasone furoate, betametasone**)

MASCC clinical practice guidelines for the prevention and management of acute radiation dermatitis: part 1) systematic review

Tara Behroozian,[a,*] Daniel Goldshtein,[b] Julie Ryan Wolf,[c] Corina van den Hurk,[d] Samuel Finkelstein,[e] Henry Lam,[f] Partha Patel,[g] Lauren Kanee,[h] Shing Fung Lee,[i] Adrian Wai Chan,[k] Henry Chun Yip Wong,[l] Saverio Caini,[m] Simran Mahal,[n] Samantha Kennedy,[n] Edward Chow,[o] and Pierluigi Bonomo,[p] on behalf of the Multinational Association of Supportive Care in Cancer (MASCC) Oncodermatology Study Group Radiation Dermatitis Guidelines Working Group

Prophylactic actions

ELSEVIER
Critical Reviews in Oncology/Hematology 96 (2015) 167–182
CRITICAL REVIEWS IN Oncology Hematology Incorporating Geriatric Oncology
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Acute skin toxicity management in head and neck cancer patients treated with radiotherapy and chemotherapy or EGFR inhibitors: Literature review and consensus

Elvio G. Russi [a,*], Francesco Moretto [b], Monica Rampino [b], Marco Benasso [c], Almalina Bacigalupo [d], Vitaliana De Sanctis [e], Gianmauro Numico [f], Paolo Bossi [g], Michela Buglione [h], Antonino Lombardo [i], Mario Airoldi [j], Marco C. Merlano [k], Lisa Licitra [g], Nerina Denaro [k], Stefano Pergolizzi [l], Carmine Pinto [m], Renè- Jean Bensadoun [n], Giampiero Girolomoni [o], Johannes A. Langendijk [p]

Not advisable:

- Topical steroidal agents (skin thinning, bacterial infections)
- Silver sulfadiazine (sensitivity with overuse)
- Aloe Vera (is not a moisturizer)

Table 5.2 General principles of skin care for head and neck patients

Patient should:	Patient should not:
• Cleanse daily with a non-perfumed mild soap and water	• Rub, put pressure on, or scratch radiated area
• Moisturize the skin	• Expose the treatment area to direct sunlight when undergoing radiation treatments
• Protect the radiated site from sun exposure by using a soft, wide-brimmed, sun blocking hat or scarf	• Take hot water showers, hot baths, use wash cloths
• Apply sunscreen with SPF >25 to exposed treatment area if in the sun. Ensure this is washed off prior to daily radiation treatment	• Use a razor in the radiation site for shaving
• Monitor weight during treatment and have access to nutritional consults, to promote wound and skin healing	• Apply astringents, facial toners, after shave lotions or colognes to the radiation site
• Remove all dressings or films, prior to treatment	• Apply any lotion, cream, or ointment in the 3 hours prior to radiation treatment
	• Wash off lotion, cream, or ointments if applied three or more hours before radiation treatment
	• Use drying agents to the skin unless instructed to do so
	• Use any tape or adhesives on the radiated skin

Fowble B. et al., *Skin care in radiation oncology,* SPRINGER 2016

Classification Scale	Scores	Clinical description
RTOG	0	No change
	1	**Erythema; dry desquamation**, epilation
NCI CTCAE v. 5.0	0	No change
	1	Faint **erythema** or **dry desquamation**

Erythema

- Cleanse daily, mild non-perfumed soap and water
- Light moisturizing lotion twice daily (avoid application 3 h prior to RT)
- Protect radiation site from exposure
- Avoid rubbing/friction to the skin surface
- Cooling compresses to brisky erythematous areas for comfort
- Mild potency corticosteroids (e.g. Mometasone furoate 0.1%) for pruritus/irritation

Dry desquamation

- Daily cleansing with NaCl 0.9%
- Manually debride peeling skin once a day (nurses)
- Moisturize twice a day (avoid application 3 h prior to RT)

Fowble B. et al., *Skin care in radiation oncology,* SPRINGER 2016



Classification Scale	Scores	Clinical description
RTOG	2	Bright erythema, **moist desquamation**, edema
	3	**Confluent moist desquamation**, pitting edema
NCI CTCAE v. 5.0	2	Moderate to brisk erythema; **patchy moist desquamation**, mostly confined to skin folds and creases; moderate edema
	3	**Moist desquamation** in areas **other than skin folds and creases; bleeding induced by minor trauma** or abrasion

1. Infection prevention
   - Cleansing with **NaCl 0.9%**
   - NO povidone-iodine
   - NO gentian violet

2. Moist wound/healing environment
   - Enhances fibroblast proliferation and keratinocyte differentiation
   - Excessive moisture detrimental

Fowble B. et al., *Skin care in radiation oncology*, SPRINGER 2016

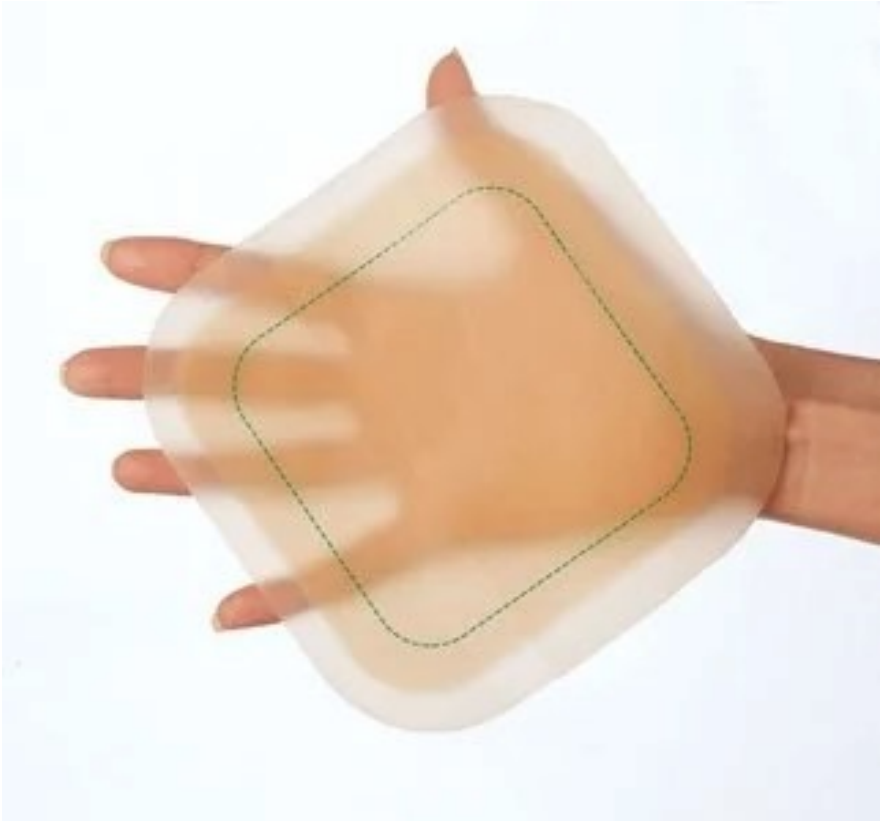
Hyaluronic acid

- Polymer that is widely distributed in connective tissues
- Key component of the dermal extracellular matrix
- Stimulate fibroblasts and fibrin development
- Benefit in delaying and diminishing the intensity of the duration of the reactions (Liguori et al., *Radiother Oncol.* 1997)

Silver sulfadiazine

- Active against gram-positive and gram-negative bacteria, including *P. aeruginosa, S. aureus, S. epidermidis*.
- Once-twice daily as a thick coating, covering the entire treatment area
- Secondary dressing necessary: avoid adhesive tapes/plasters, use elasticated tubular bandage
- Prior to each new application, previously placed one should be clean away along with tissue debris: pain and alteration of the healing process

Fowble B. et al., *Skin care in radiation oncology,* SPRINGER 2016



Hydrocolloids

- Hydrophilic colloid particles bound to polyurethan foam
- Impermeable, adherent, yellow, malodorous gel in contact with the surface of the wound (looks like infection)
- Complete barrier properties
- Inappropriate for daily removal
- Appropriate for relatively dry wounds

Zasadzinski K. et al., *Pharmaceutics* 2022

Film dressings

- Adhesive (not on moist desquamation), porous and thin transparent polyurethane
- O_2, CO_2, H_20 vapor from the wound pass through the dressing
- Liquids and bacteria are well-isolated
- Suitable on epithelializing **superficial wounds with few exudates**

Zasadzinski K. et al., *Pharmaceutics* 2022

Foam dressing

- Polyurethane or silicon-based
- Semipermeable, with a bacterial barrier
- Thermal insulation, moisture to the wound
- Prevent damage to the wound at the time of removal
- May be used as secondary dressing with hydrogel/alginate dressing
- Suitable for handling moderate-to-high volumes of wound exudate
- Favored over aqueous creams/standard wound care in 3 RCTs (Paterson et al., *J Cancer Sci Ther* 2012, Diggelmann et al., *BJR* 2014, Zhong et al,. *Med Oncol* 2013)

Zasadzinski K. et al., *Pharmaceutics* 2022

Hydrofibers, calcium alginate dressings, silver-impregnated dressings

- May absorb 10-15 times their weight
- Only appropriate for heavily exudative wounds
- Non-traumatic removal as a gel-forming dressing
- Hemostatic properties
- Silver does not tend to produce resistance
- No evidence supports one product over another

Crustose exudations

Debridement of crusts may help to reduce the risk of super-infections and bleeding

Zasadzinski K. et al., *Pharmaceutics* 2022
European Oral Care in Cancer Group, Oral Care Guidance and Support 1st ed

4.6. Infection management

1. 4.6a. Consider topical or systemic antimicrobials if positive cultures or documented infections are present.
2. 4.6b. An empirical systemic antibiotic therapy must be used as soon as possible when two altered parameters of Systemic Inflammatory Response Syndrome (SIRS) and/or other signs of systemic inflammatory response to infection (such as inflammatory, haemodynamic, organ dysfunction and tissue perfusion parameters [147,148]) coexist with a suspected infection.

SIRS parameters need monitoring. Indeed, even if two positive SIRS parameters are not specific of sepsis [148–150], they may help physicians to graduate the urgency of intervention, to promptly activate the search for infection and for other signs of systemic inflammatory response to infection (such as inflammatory, haemodynamic, organ dysfunction and tissue perfusion parameters [147,148]), in order to shorten the time to start antibiotic administration [151].

In cases of dermatitis of grade 2/3, when a superinfection is suspected without systemic-inflammatory-response involvement, antiseptics and/or topical antibiotics (such as clindamycin and erythromycin) may be helpful, but it might be useful to obtain an antibiogram of exudative lesions.

If serious toxicity is associated to a systemic inflammatory response, culture data should be obtained before starting any empirical antibiotic treatment [151].

SIRS criteria
- Temperature > 38 C or < 36 C
- Heart rate > 90 bpm
- Respiratory rate > 20 breaths per minute or $PaCO_2$ < 32 mmHg
- White blood cell count > 12000/mcL, < 4000/mcL or > 10% immature (band) forms

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Acute skin toxicity management in head and neck cancer patients treated with radiotherapy and chemotherapy or EGFR inhibitors: Literature review and consensus

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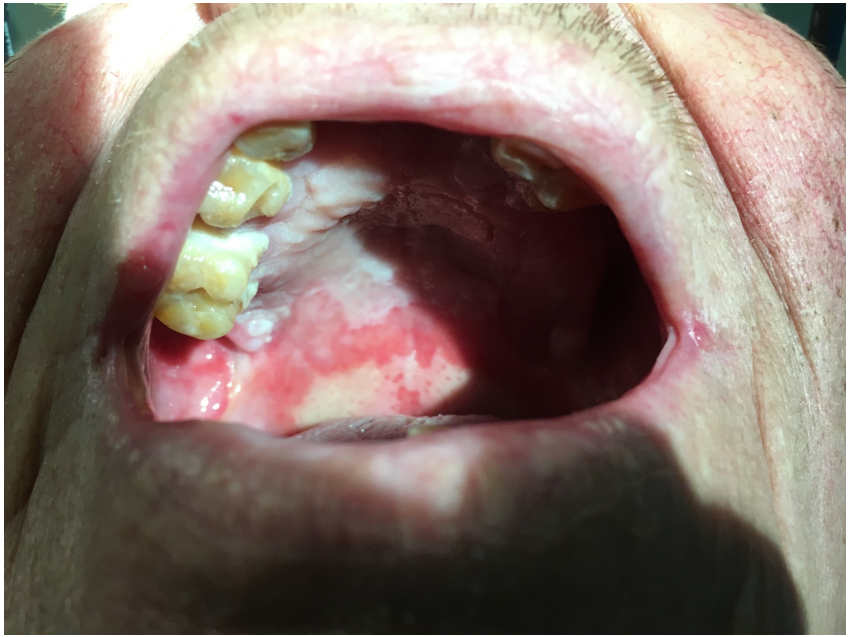
ORAL MUCOSITIS



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- Associated with pain, difficulty in eating and swallowing, the need for enteral nutrition, increased opioid consumption, **interruptions to cancer therapy**
- In immunosuppressed patient, it is associated with bacteremia, increased inpatient hospitalization duration, and higher 100-day mortality.

clinical practice guidelines

Annals of Oncology 26 (Supplement 5): v139–v151, 2015
doi:10.1093/annonc/mdv202
Published online 4 July 2015

Management of oral and gastrointestinal mucosal injury: ESMO Clinical Practice Guidelines for diagnosis, treatment, and follow-up†

D. E. Peterson[1], C. B. Boers-Doets[2], R. J. Bensadoun[3] & J. Herrstedt[4], on behalf of the ESMO Guidelines Committee*

Table 1 Example of a Basic Oral Care Protocol (expert opinion)

Two key strategies for mitigation of oral mucosal injury before and during treatment are	
•Maintenance of optimal nutritional support throughout the entire period of cancer therapy.•Developing a daily oral hygiene routine, including brushing teeth and the gums four times a day with a soft brush and using mouth rinses. This approach can contribute to the reduction and, ideally, prevention of oral tissue injury and associated pain, nutritional compromise, and related adverse outcomes.	
The following information is presented as a portfolio of patient-based instructions for which health professional guidance is recommended	
General measures	•Inspect your oral mucosa daily.•Have your dental team eliminate sources of trauma (e.g. ill-fitting prostheses; fractured teeth).•Lubricate lips with (sterile) vaseline/white paraffin (petrolatum), lip balm, or lip cream. Be aware that vaseline/white paraffin (petrolatum) should not be used chronically on the lips, as this promotes mucosal cell dehydration and is occlusive leading to risk of secondary infection.•Drink ample amount of fluids to keep the mouth moist.
Brushing teeth and gums	•Use a soft toothbrush or swab (as tolerated) after meals and before sleep. Brushing with a soft toothbrush reduces risk of bleeding. Each month you should utilise a new soft toothbrush.•Clean the dentition and gingiva with a mild fluoride-containing, non-foaming toothpaste.•Brush teeth twice a day (after meals and at bedtime) according to the Bass or modified Bass method. If using an electric toothbrush, utilise the techniques cited in the product description instead.•Rinse the brush thoroughly after use with water and store the toothbrush in a cup with the brush head facing upward.•If you are used to do so, clean the area between the teeth once a day. Consult a dental hygienist/dentist about the most appropriate interdental cleaner (floss, toothpick, brushes). In case you are not used to use interdental cleaners on a regular base, do not start with it while on cancer therapy, since it can break the epithelial barrier, visible through gingival bleeding.
Rinse mouth	•Rinse mouth with an alcohol-free mouthwash upon awakening and at least four times a day after brushing, for ~1 min with 15 ml mouthwash; gargle; and then spit out. During the first half hour after rinsing, avoid eating and drinking.
Denture care	•Remove dentures before performing oral care. Brush dentures with toothpaste and rinse with water; clean the gums.•Defer wearing dental prostheses as much as possible until the lining tissues of your mouth are healed. If in the hospital, soak the denture for 10 min in an antimicrobial solution (e.g. chlorhexidine 0.2% if available) before inserting in your mouth.
Avoid painful stimuli	•Smoking•Alcohol•Certain foods such as tomatoes, citrus fruits, hot drinks and spicy, hot, raw, or crusty foods.

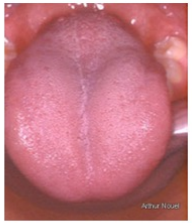
Fig: 3 Sites to be examined


Upper inner inside of the lip


Lower inner inside of the lip


Left and right inner inside of the cheek


Soft palate


Tongue dorsal


Tongue right and left lateral


Floor of the mouth and ventral

First Edition

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7 APRIL 2017

European Oral Care in Cancer Group
Oral Care Guidance and Support

Classification Scale	Scores	Clinical description
RTOG	1	Irritation/may experience mild pain not requiring analgesic
NCI CTCAE v. 5.0	1	Asymptomatic or mild symptoms; intervention not indicated

- Basic oral protocol
- Baking soda/saline mouthwash
  - E.g. Rinse 5-6 x/day with ½ teaspoon (2.5g) salt and 2 tablespoon (30g) baking soda in 1 liter water
- **Benzydamine** 0.15% mouthwash, 15 ml rinse or gargle (> 30 s, not to be swallowed)
  - Recommended for RT
  - *Suggested for CRT*
- Sucralfate (combined topical and systemic) is **not recommended** for the prevention/treatment of OM-associated pain in H&N patients treated with RT

Elad S. et al., *Cancer* 2020

Classification Scale	Scores	Clinical description
RTOG	2	**Patchy** mucositis that may produce an inflammatory serosanguinous discharge/may experience moderate pain **requiring analgesia**
	3	**Confluent fibrinous mucositis**/may include severe **pain requiring narcotic**
NCI CTCAE v. 5.0	2	Moderate pain; **not interfering with oral intake; modified diet indicated**
	3	Severe **pain**; **interfering with oral intake**

- Basic oral protocol
  - Baking soda/saline mouthwash
  - Benzydamine 0.15% mouthwash, 15 ml rinse or gargle (> 30 s, not to be swallowed)
- **Viscous lidocaine 2%** (max 300 mg/dose, max 8 dose/day; interferes with Sucralfate, > 30 min)
- **Morphine 0.2%** mouthwash (suggested per MASCC guidelines, no coating agent showed a benefit when compared).
- No suggestion is possible for *topical steroids* use; systemic continuous employment of steroidal therapy for mucositis prevention/treatment is not recommended

Elad S. et al., *Cancer* 2020
AIOM 2014
De Sanctis V. et al., *Crit Rev Oncol Hematol* 2015

- **Oral candidiasis**
  - Nystatine suspension, 4-6 ml swish and swallow tid-qid. Continue 2 days post-symptom resolution
  - Miconazol, 1 film tablet/day applied on the upper gum (30s) for 7-14 days. *If the film tablet falls/is swallowed within the first 6 hours, drink a glass of water and apply another one*

First Edition

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- **Thick secretions**
  - Steam inhalation or nebulizers may help loosen them. Normal saline or sodium bicarbonate solutions may be used
- **Bleeding**
  - Mouth washes
  - Tranexamic acid, 500 mg as mouth wash (gargling/swishing), can be considered
- **Dry mouth**
  - Saline mouth washes
  - Xylitol-based chewing gum
  - Oral lubricants

RHINOSINUSITIS

Fang et al., *Front. Oncol.* 2022

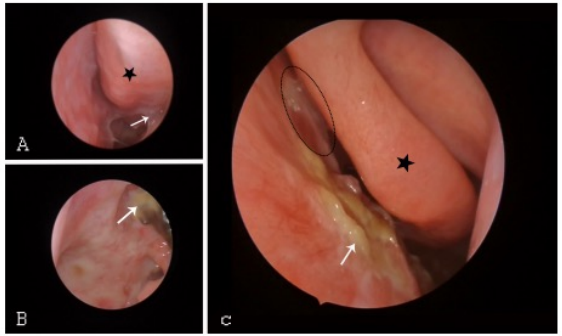

FIGURE 2
Endoscopic changes in NPC patients after RT. **(A)** Black star: congested IT. White arrow: adhesions throughout the nasal tract. **(B)** White arrow: pharyngeal fossa in the nasopharynx. **(C)** Black asterisk: MT. White arrow: middle nasal tract with purulent secretions and scabs. Black ellipse: middle nasal tract with nasal adhesions. IT, inferior turbinate; MT, middle turbinate.

FIGURE 1
Nasal manifestations after RT in NPC patients.

- Dilatation of the nasal passages with a petroleum-coated cotton swab until mucositis has resolved prevents the formation of nasal cavity synechiae
- Saline nasal spray can symptomatically manage dry mucous membranes

Halperin et al., *Perez & Brady's Principles and Practice of Radiation Oncology,* LWW 2018

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Radioterapia Oncologica:
l'evoluzione al servizio dei pazienti

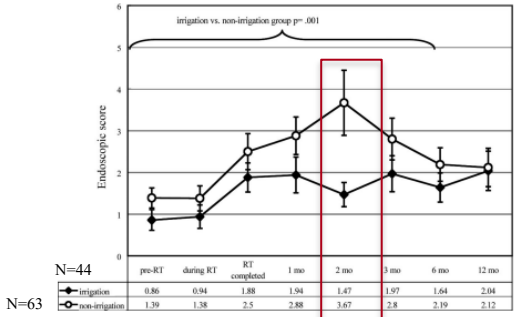

Figure 1. The mean endoscopic scores of patients in the irrigation group and nonirrigation group.

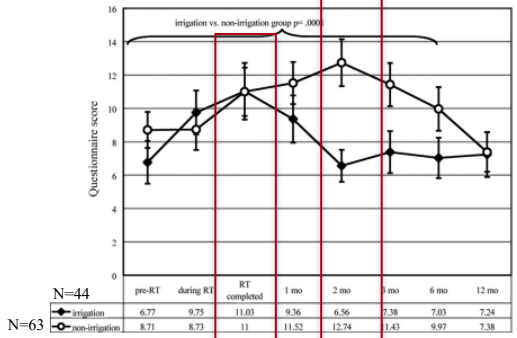

Figure 2. The mean questionnaire scores of patients in the irrigation group and nonirrigation group.

Liang et al., *Am J Rhinol* 2008

Item	Group A	Group B	Group C	λ^2 value	*p*-value
Incidence of nasal sinusitis at each time point					
Baseline	179 (378)	158 (378)	136 (378)[a]	10.060	0.007
Time a	212 (372)	198 (365)	213 (369)	1.000	0.606
Time b	216 (336)	227 (317)[a]	301 (352)[a,b]	41.690	0.000
Time c	138 (283)	154 (274)	175 (307)[a]	4.770	0.092
Time d	112 (206)	161 (197)[a]	156 (213)[a,b]	37.630	0.000

The numbers enclosed by parentheses indicate the total number of questionnaires completed.
[a]Significant difference from Group A.
[b]Significant difference from Group B.

Item	Time (after RT)
a	6 m
b	1y
c	2y
d	3y

Item	Group
A	Disposable nasal irrigator
B	Homemade nasal irrigator connector combined with an enemator
C	Nasal sprayer

Luo et al., *Br J Radiol* 2014


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