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內文：

I. Abstract:

1. The exposure to high doses of ionizing radiation during radiotherapy results in severe morphological and functional alterations of the salivary glands, such as xerostomia. Investigated the chronic effect of a single radiation dose of 15 Gray (Gy) limited to head and neck on rat salivary gland function (salivary secretion and gland mass) and histology.
2. Results indicate that norepinephrine (NE)-induced salivary secretion was reduced significantly at 30, 90, 180 and 365 days after ionizing radiation. The maximal secretory response was reduced by 33% at 30 and 90 days post irradiation. The functional fall of the salivary secretion observed at 180 days post irradiation was not only associated with a reduction of gland mass but also to an alteration of the epithelial architecture exhibiting a changed proportion of ducts and acini, loss of eosinophilic secretor granular material, and glandular vacuolization and fibrosis.

II. INTRODUCTION:

1. Radiotherapy is a central treatment modality administered for head and neck cancers. Salivary glands are unavoidably irradiated causing devastating side-effects including severe gland functional and structural alterations which result in salivary dysfunction and consequent irreversible xerostomia. (“dry mouth”)
2. Salivary glands consist of several cell types: acinar cells which are responsible for water and protein secretion, myoepithelial cells surrounding the acini and ducts, and ductal cells which mainly modulate the ionic composition of the saliva.
3. Ionizing radiation induces apoptosis and proliferation during the early post radiation phase in submandibular gland (SMG) acini and ducts of the mouse. The imbalance between apoptosis and proliferation causes the impairment of the SMG during the late radiation damage in the mouse. The increased apoptosis is the main cause of the imbalance.
4. We investigated the chronic effect of a single radiation dose of 15 Gy limited to head and neck on salivary gland function (salivary secretion and gland mass) and histology.

III. MATERIAL AND METHODS

1. Animals:
   Adult female Wistar rats (250-300 g), lights on from 6 AM to 8 PM and 22-24 °C. Divided into several experimental groups with 6-8 animals each.
2. Irradiation:
   Anaesthetized (Ketamine 10mg/kg and Xylazine 8mg /Kg, i.m.) rats were irradiated to the head and neck region with a single non lethal dose of

gamma ray radiation of 15 Gy using a gamma-ray apparatus (Theratron 780) with 60 Cobalt bomb at a dose rate of approximately 1 Gy/min with an 80 cm source to skin distance.

Control animals were anaesthetized but not exposed to radiation.

3. Determination of Salivary Response:

At 2 h, and 30, 90, 180 and 365 days post radiation exposure in rats under anesthesia (chloralose 100 mg/kg 0.5 ml NaCl (0.9%), i.v.).

The right femoral vein was cannulated with a polyethylene catheter (P40 catheter, Rivera & Cia, Argentina) to administered the sialagogic agonist, norepinephrine (NE)

Salivation was induced by the administration of different concentrations of NE ranging from the threshold dose to the dose that exerts the maximum stimulus (0.3, 1, 3, 10 and 30μg/kg, in saline)

4. Body and Glandular Weight Measurement:

Body weight was measured at 2 h, and 30, 90, 180 and 365 days post radiation exposure. The SMG were dissected and weighed (wet glandular weight). The SMG were put in a dry stove during 12 h at 180 °C and then weighed.

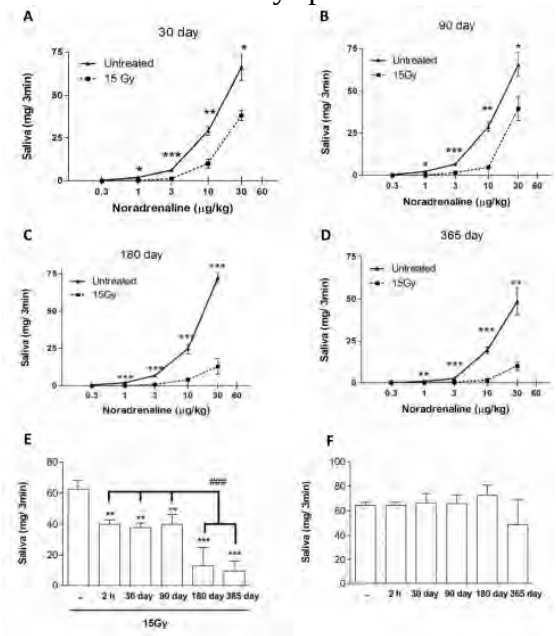
5. Histopathological Studies:

Fixed with 10% neutral buffered formalin. Mucous and serous acini and intercalated and striated ducts were counted in rats after 180 days post radiation and were expressed by number of elements per 100x-magnification field.

IV. RESULTS

1. Chronic Effect of Ionizing Radiation on Salivary Secretion:

The maximal response to NE was diminished by 33% in 30 days post irradiated rats in comparison to that of non-irradiated rats. The percentage of diminution was maintained at 90 days post radiation exposure and was not significantly different from the salivation reduction observed after 2 h post irradiation. After 180 days post irradiation a new fall in the salivary secretion was observed showing a 75% reduction in the maximal response to NE in comparison to non-irradiated animals. This decrease was maintained in 365 days post irradiated rats.



2. Chronic Effect of Radiation on Body and Glandular Weights:
Reduction of about 12 % was observed in the body weight of rats after 30, 90 and 180 days post irradiation in comparison to non-irradiated animals. A further decrease was demonstrated in irradiated animals after 365 days (22%)
Glandular weight: Proportional changes in both wet and dry weights, showing 23-25 %, 27 % and 43-49 % reduction in 90, 180 and 365 days post irradiated rats. To better understand the effect of radiation on glandular mass we compared the SMG wet weight as a percentage of body weight. A Significant reduction of SMG wet weight relative to body weight was observed in irradiated animals after 180 and 365 days post irradiation.

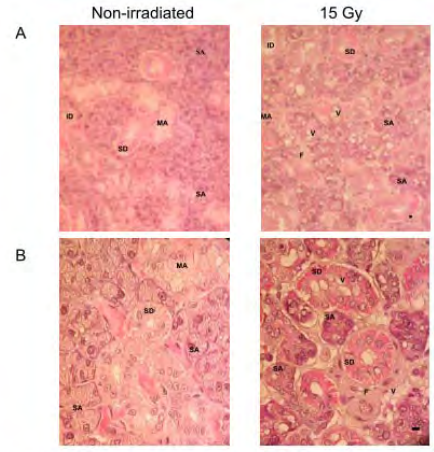


Fig. (2). Histological appearance of non-irradiated and 15 Gy dose irradiated SMG at 180 days. (**A**) 100x magnification. (**B**) 400x magnification. Scale bar 20 µm. MC: mucous acinos. SA: serous acinos. SD: striated duct. ID: intercalary duct. SD: striated duct. F: fibrosis. V: vacuoles.

3. Effect of Ionizing Radiation on SMG Morphology:
Functional break at 180 days post irradiation, so we evaluated the histology of the gland at the same time. The number of serous and mucous acini per field was significantly reduced in SMG derived from 180 days post irradiated in comparison to non-irradiated animals. Increase in the number of striated ducts per field at 180 days post irradiation, this could be due to the diminution in the number of acini that facilitated the striated ducts over-expression

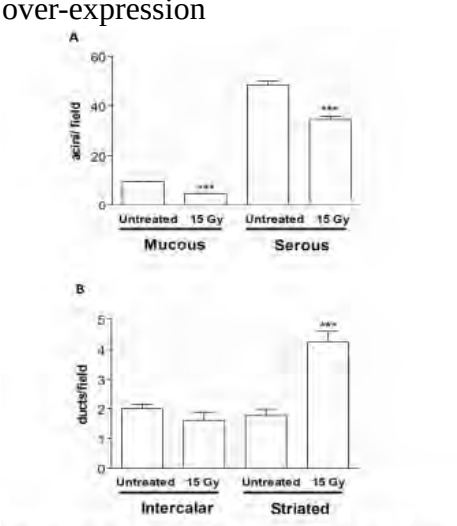


Fig. (3). Number of mucous and serous acini per field (**A**) and number of intercalated and striated ducts per field (**B**) in SMG of 180 days post irradiated rats. Values represent means ± SEM of 6-8 animals per group. ***p<0.01 versus respective control.

V. DISCUSSION

1. This pathological condition in humans is manifested by oral dryness, impairment of normal oral functions (speech, chewing, and swallowing) because of insufficient wetting, and decreased lubrication of the mucosal surfaces and of ingested food. Furthermore, the oral mucosa can become dry and atrophic, leading to frequent ulceration and injury (Fig. 4A and B). Finally, the shift in the oral microflora towards cariogenic bacteria, the reduced salivation.

2. The chronic secretory hypo-function observed could be not only due to alterations in the functional capability but also to progressive tissue damage that leads to a reduction of glandular mass.
3. Late damage to the DNA leads to a diminution of mitotic velocity. This takes place at 90 days post irradiation. The increase of apoptotic cells in the SMG just an hour after the irradiation.
4. We also observed a decline in SMG cell proliferation evaluated by the incorporation of the timidine analog, bromo-2'deoxyuridine (data not shown).
5. The ionizing radiation produced the loss of reparatory capability of the tissue that leads progressively to the atrophy of the gland. 180 days post irradiation was not only associated with a reduction of gland mass but also to an alteration of the epithelial architecture exhibiting a changed proportion of ducts and acini, loss of eosinophilic secretor granular material, and glandular vacuolization and fibrosis.

VI. Conclusion:

Ionizing radiation produces irreversible and progressive alterations of submandibular gland function and morphology that leads to a severe salivary hypo-function.

題號	題目
1	Salivary glands哪一種細胞類型是負責調節唾液中離子的比例？ (A) acinar cells (B) myoepithelial cells (C) ductal cells
答案(C)	出處：本篇Journal
題號	題目

2	以下何者不是頭頸部做Radiotherapy的副作用 (A) xerostomia (B) dysphagia (C) diarrhia (D) gustatory dysfunction
答案(C)	出處：本篇Journal