EVALUATION OF MUCOCILIARY ACTIVITY IN MAXILLARY ANTRA IN PATIENTS WITH SQUAMOUS CELL CARCINOMA OF BUCCAL MUCOSA UNDERGOING POST OPERATIVE RADIOTHERAPY

By

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Dissertation submitted to the

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In partial fulfilment of the requirements for the degree of

MASTER OF SURGERY

IN

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Under the guidance of

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LIST OF ABBREVIATIONS

AJCC	American Joint Committee against Cancer
BM	Buccal mucosa
CaCC	Calcium ion activated chloride channel
CECT	Contrast enhanced computerized tomography scan
CFTR	Cystic fibrosis transmemberane conductance regulator
CT	Chemotherapy
EBRT	External beam radiotherapy
ENaC	Epithelial sodium channel
FESS	Functional endoscopic sinus surgery
FNAC	Fine needle aspiration cytology
GBS	Gingivobuccal sulcus
HPE	Histopathological examination
MCC	Mucociliary clearance
MMA	Middle meatal antrostomy
MRI	Magnetic resonance imaging scan
MTT	Methylene blue transit time
NACT	Neoadjuvant chemotherapy
N-DRC	Nexin dyenin regulatory complex
PNS	Para nasal sinus
RMT	Retromolar trigone
RT	Radiotherapy
SCC	Squamous cell carcinoma
STT	Saccharin transit time
USG	Ultrasonography scan

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ABSTRACT

Background: 30-35% of malignancies in India involve head and neck region. Oral cancer accounts for about 50 % of these malignancies.[1,2] There is a high prevalence of buccal mucosa malignancy in Kolar district due to the habit of betel nut and tobacco chewing and the use of quid.

Radiotherapy is a key component in the multidisciplinary treatment used in all head and neck cancers. The underlying cause of sinusitis in irradiated patients was proven to be decreased mucociliary clearance in the nasal cavity and paranasal sinuses.[7] Even though field of radiation during Radiotherapy for squamous cell carcinoma buccal mucosa does not directly involve paranasal sinuses ,radiation sequelae in mucociliary clearance may occur in maxillary antrum on the ipsilateral side as it is a site close to the primary tumour bed.[8]

Aims and objectives:

1. To perform bilateral middle meatal antrostomy at the time of surgery to facilitate periodic nasal endoscopy to study and document mucosal changes in bilateral maxillary antra in patients with squamous cell carcinoma of buccal mucosa undergoing post-operative radiotherapy.
2. Compare mucociliary clearance in ipsilateral and contralateral maxillary antra in above mentioned patients.

Materials and methods : This study was done on patients presenting in stages $T_{3,}$ T_{4a} who require composite resection and post-operative radiotherapy during Dec 2015-Jul 2017. Patients were selected based on the inclusion and exclusion criteria.

The effects of radiation on mucociliary clearance was measured through two parameters namely Methylene blue Transit Time and Saccharine Transit Time through periodic nasal endoscopic examination performed at various intervals [just before starting radiotherapy, weekly during radiotherapy and 1 and 3 months post radiotherapy]. Bilateral middle meatal antrostomy is performed during the main surgical procedure to facilitate such measurements in the maxillary antra.

Results: Statistically significant elevation of mucociliary clearance times [Methylene blue Transit Time and Saccharine Transit Time] when compared between pre radiation values and values during radiation and follow up in maxillary antra on the side of radiation. Even though few elevated clearance times are observed in non radiotherapy side, overall clearance times on contralateral side remain un affected by radiation.

Conclusion: Our study establishes that the mucociliary clearance in maxillary antrum adjacent to the field of radiation in post operative buccal mucosa carcinoma patients, is notably affected. It should be taken into consideration that the reversal of radiation induced changes takes much longer so, dependant drainage procedures should be considered in such symptomatic individuals.

INTRODUCTION

INTRODUCTION

30-35% of malignancies in India involve head and neck region. Oral cancer accounts for around 50 % of these malignancies.[1,2] There is a high prevalence of buccal mucosa malignancy in Kolar district due to the habit of betel nut and tobacco chewing and the use of quid.

Radiotherapy is a key component in the multidisciplinary treatment used in all head and neck cancers. It is associated with many complications and sequelae out of which sinusitis is one. It needs regular assessment as a part of followup.[3,4,5,6]

The underlying cause of sinusitis in irradiated patients was proven to be decreased mucociliary clearance in the nasal cavity and paranasal sinuses.[7]

Even though field of radiation during Radiotherapy for squamous cell carcinoma buccal mucosa does not directly involve paranasal sinuses ,radiation sequelae in mucociliary clearance may occur in maxillary antrum on the ipsilateral side as it is a site close to the primary tumour bed.[8]

External beam irradiation therapy (megavoltage) using cobalt 60 machine is used for post operative cases of squamous cell carcinoma buccal mucosa in our hospital as there is no access to Intensity Modulated Radiotherapy.

Study was designed to perform bilateral middle meatal antrostomy and study and document mucociliary clearance in patients receiving post operative radiotherapy for squamous cell carcinoma of buccal mucosa. Based on the findings it may help future studies to decide

between middle meatal antrostomy or inferior meatal antrostomy which is in a dependant position in preventing post irradiation rhinosinusitis.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

HISTORY OF HEAD AND NECK CANCER:

Head and neck cancer is a primitive disease. Evidence of nasopharyngeal carcinoma in Egyptian skulls dating 3000 BC has been described.[9]Around the same period in the ancient text of Ebers papyrus contains description of an 'ulcer eating the gums'.[10] Doctrine of Hippocrates was the first text to use the term carcinoma and its recommended treatments.[11]

Aurelius Cornelius Celsus (30AD) had first documented treatment of cancer of face and lip in ancient roman texts. Galen (150 AD) considered cancer to be systemic disease, this has discouraged local treatment for tumours. Later on Descartes(17 th century) replaced galen's "black bile" theory with a mechanistic lymph theory. This paved a way for lymph node dissection. First cancer hospital was established in France by Jean Godinot in 1740

Tobacco was started to be widely used during mid 16th and 17th century. John hill (1761) implicated that tobacco causes cancer.[12] Later on many others made observations on chimney smoke, pipe smoking , tobacco sniffing leading to cancer.[13,14]

19th century is considered the dawn of scientific medicine as many breakthroughs in anaesthetic techniques ,antisepsis, diagnostic tools , surgical therapies and understanding pathological mechanisms took place. Roentgen discovered X rays on 30 November 1895 which was followed by description of phenomenon of radioactivity by Bequerel. Curies discovered radium in 1898.[15] Radiation therapy evolved to the more exact science it is today through the history.From initial measurements of radiation based on its effects on skin to the current strategies of treatment planning based on anatomical constraints and dosimetry.[16,17]

Radiation was first administered through radium needles and implantation of 'seeds', later on externally delivered radiation became available. Coutard and Baclesse were the pioneers of radiation techniques. Coutard has laid guidelines for duration of radiation treatment based on size of tumour.[18]

Conventional X-ray was used initially as a method for delivering external beam radiation. Improvised methods like ^{60}Co units, 2 MeV generators and electron beams were used in 1950s and later linear accelerators were developed. These newer modalities were able to target deeper areas of tumours and minimize damage to skin and uninvolved structures. The art of radiation therapy is to find optimal dose for cure with minimal side effects.[19]

Radiation soon became the preferred modality until the era of second world war since even after heroic efforts of surgeons the morbidity and mortality rates were high and surgery could be extremely disabling. By mid 20th century limitations of using radiation as a single modality treatment became obvious and radiation as an adjunct to surgery came into use.[19]

Newer techniques like intensity modulated radiotherapy, hyperfractionation and radiosensitizing chemotherapeuticshave revolutionized radiation therapy in head and neck cancers.

ICRU(International Commission on Radiation Units) in 1953 has replaced the "R" (roentgen) with "rad"(radiation absorbed dose) which was in use till 1985. Later "Gy" (Gray, named after Harold Gray a british physicist) has been in use till today .1 Gy is equal to 100 rad.[19]

Surgical approaches to various head and neck cancers like tongue,oral cavity,larynx were developed by the great surgeons of the time like Billroth,Kocher,Von Langeback,Von

Volkmann.When it comes to approaches for oral cavity tumours Kocher introduced approach through submandibular region.Langeback, Billroth and others have introduced lip split and midline mandible sectioning approach.[20,21]

Even though George crile Sr and Sir Henry Butlin have addressed the important issue of nodal metastasis by neck dissection , radiation therapy for head and neck cancers became the' holy grail' until 1940s as surgery had significant complication and comorbidity.[22,23] Butlin with Wolfer started the concept of 'in-continuity' removal of primary oral tumour with upper cervical lymph nodes. Sir Henry Butlin was the one who stated smoking is a definitive causal factor for cancer of tongue.[24]

In 1940s Hayes Martin started performing a procedure called 'commando operation' approach being midline lip split ,segmental mandibulectomy and in-continuity radical neck dissection.[25] In 1952 Sua´rez developed the technique of Modified radical neck dissection which involves dissection of lymph node levels I – V with preservation of non involved structures such as the internal jugular vien , sternocliedomastoid muscle and accessory nerve. later on Alando J. Ballantyne popularized this technique. The concept of selective neck dissection was given by Byers.[26,27,28,29,30]

During the 1950s and 1960s, the emphasis shifted from the excision of tumour to excision of tumour combined with the reconstructive aspect of surgery

Important pioneers and contributors in this field are listed below:

- 1951 A.D. -- Edgerton advocated the use of skin graft.[31]
- 1956 A.D. -- Klopp and Schurter described the local tongue flap.[32]
- 1957 A.D. -- Edgerton and D'Perez described Submandibular apron flap.

- 1963 A.D. -- Deltopectoral flap (medially based) was described by Bakamjiam.[33]
- 1979 A.D. -- Stephan Ariyan described the pectoralis major myocutaneous flap based on the pectoral branch of the thoraco- acromial artery. This is 'the work horse' of the head and neck reconstruction surgery.[34]

The forehead flap has been in use for a long time and was first described by McGregor, who advocated its use for resurfacing of the oral cavity.[35,36] There are a wide range of 'free flaps' available, but among them important ones are the free osteomyocutaneous groin flap, osteomyocutaneous rib flaps and also the radial forearm flap termed as 'The Chinese flap' developed by Dr. Yang Goufan, Chen Baoqui and Gao Yucht of the Shenjeing military hospital, in 1978.[37]

ANATOMY OF ORAL CAVITY

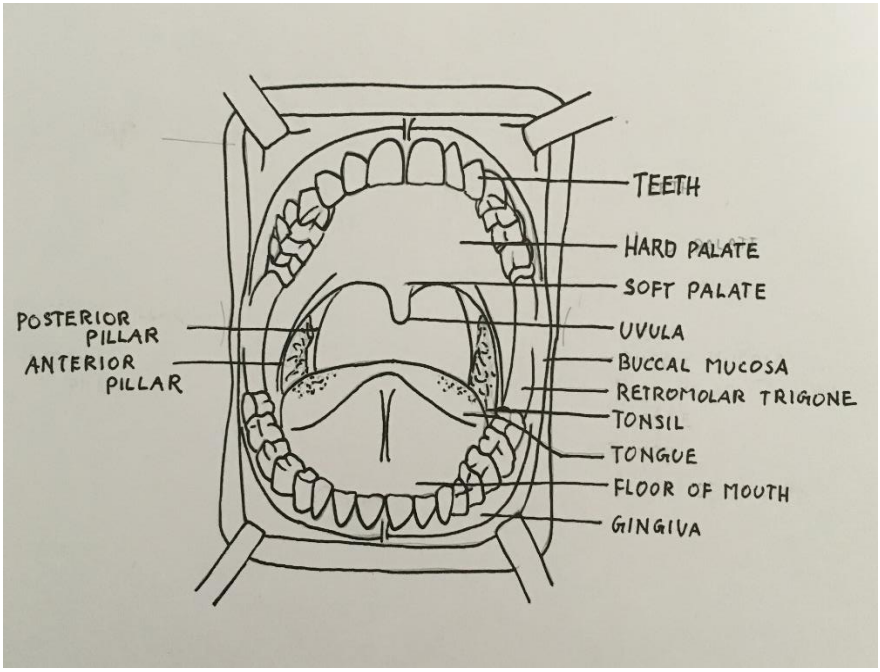


Fig.1. oral cavity anatomy

Oral cavity extends from the vermilion border of lips anteriorly to the oropharyngeal isthmus posteriorly.

This comprises the circumvallate papillae on the dorsum of the tongue, anterior pillars on either side and superiorly to the junction of hard and soft palate.[38]

Subsites:

- upper and lower dento alveolar ridge
- anterior 2/3rd of tongue
- floor of mouth
- buccal mucosa
- retromolar trigone
- mucosa of lips
- hard palate

LYMPH NODES IN THE NECK:

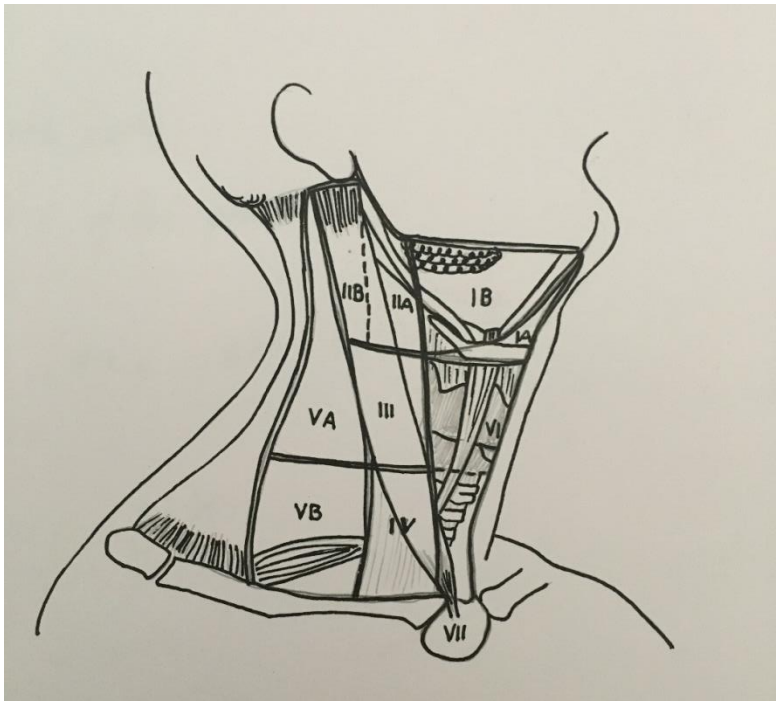


Fig 2. picture showing lymphnode levels of the neck

LEVEL 1:

Submental and submandibular groups:

The submental lymph nodes (level 1A) refer to the nodes lying within the submental triangle. The submandibular lymph nodes (level 1B) are defined as those contained within the submandibular triangle.

LEVEL 2:

Upper jugular nodes:

The level 2 lymph nodes are located around the upper third of neck, extending from carotid bifurcation (surgical landmark) or hyoid bone (clinical landmark) to the skull base, laterally bounded by posterior border of sternocleidomastoid , medially by lateral border of posterior

belly of digastric muscle, anteriorly by posterior border of ramus and angle of mandible and a line joining angle of mandible to greater horn of hyoid.

Level 2 is further divided into two zones by the spinal accessory nerve. Level 2a is located anterioinferior to the nerve and level 2b is located posterosuperior to the nerve.

LEVEL 3:

Mid jugular nodes:

Level 3 nodes are located around middle third of internal jugular vein.

Boundaries:

Superiorly- carotid bifurcation/ hyoid bone

Inferiorly – omohyoid muscle

Laterally- posterior border of sternocleidomastoid

Medially- lateral border of sternohyoid muscle

LEVEL 4:

Lower jugular nodes:

Located around lower third of neck.

Boundaries:

Superiorly- omohyoid muscle/ cricoid cartilage

Inferiorly- clavicle

Laterally- posterior border of sternocleidomastoid muscle

Medially- lateral border of sternohyoid muscle.

It can be further divided into:

4a :lymph nodes located beneath sternal head of sternocleidomastoid

4b: lymph nodes located beneath clavicular head of sternocleidomastoid

Level 5:

Posterior triangle lymph nodes:

Lymph nodes located along lower half of spinal accessory nerve and transverse cervical artery.

Divided into:

5a: lymph nodes located above inferior belly of omohyoid muscle

5b: lymph nodes located below inferior belly of omohyoid muscle.

Level 6 :

anterior compartment lymph nodes

boundaries:

superiorly – hyoid bone

inferiorly – suprasternal notch / innominate artery

laterally- bounded by carotid artery on either side

Level 7:

upper anterior mediastinal lymph nodes.[39]

ANATOMY OF NOSE

EXTERNAL NOSE

External nose is shaped like a triangular pyramid with its root above and base directed inferiorly. In the base there are anterior nares, separated by a median septum. The lower part of each side of external nose has a rounded eminence, the ala nasi , which forms the outer boundary of the nostril. The nasal bones form the bridge, and each is united above with frontal bone and laterally to frontal process of maxilla. Two paired cartilages, the upper and lower lateral cartilage and one unpaired cartilage, the septal, complete the external framework. The chief muscles acting of nose external nose are the compressors and dilators of ala nasi supplied by facial nerve.

Blood supply to the external nose is from maxillary and ophthalmic arteries.

The anterior facial vein and ophthalmic vein forms the venous supply, lymphatics drain to the submandibular and pre-auricular lymph nodes. The skin of external nose receives its sensory supply form the two upper divisions of the trigeminal nerve; ophthalmic and maxillary.[40]

NASAL CAVITY

Each nasal cavity is divided into three parts i.e., nasal vestibule, olfactory region and respiratory region. Nasal vestibule is the most anterior and it extends from the nostril antero-inferiorly to the nasal valve postero-superiorly. The nasal valve is situated between the caudal end of the upper alar cartilage laterally and the septum medially. The area of demarcation is limen nasi, with skin containing hair follicles, sebaceous and sweat glands. It

is a space of importance since it is here that nasal cavity is the narrowest, limited to a triangular shape of only 0.3 cm^2 on each side.

The olfactory region is confined to the upper part of the nasal cavity and the superior turbinate representing an area of 10 cm^2. The rest of the nasal cavity constitutes the respiratory region and its surface may reach 120 cm^2.

The lateral wall of each nasal cavity has superior, middle, and inferior turbinates. Each turbinate overhangs a meatus. The space below or medial to superior turbinate is spheno-ethmoidal recess to which sphenoidal sinus open. The posterior ethmoidal cells drain into the superior meatus. The anterior ethmoidal, frontal and maxillary sinuses open into middle meatus. The nasaolacrimal duct opens into inferior meatus.

Middle meatus contains several structures of importance. An enlargement is found at anterior end of the middle meatus, which is a part of ethmoidal bone, called as uncinate process. A little further back is another eminence which is called bulla ethmoidalis, which represents a protrusion into the meatus of one of the air cells of the ethmoidal labyrinth. Between these two enlargements is a groove which is known as hiatus semilunaris which leads to a narrowing called infundibulum.

Arterial supply is via the lateral branches of sphenopalatine, greater palatine, superior labial, anterior and posterior ethmoidal arteries. venous drainage occurs through the pterygoid plexus. Lymphatics drain into the submandibular nodes anteriorly and to the lateral pharyngeal, retropharyngeal and upper deep cervical nodes posteriorly.

Main sensory supply to the nasal cavity is derived from maxillary division of trigeminal nerve through branches arising in pterygopalatine ganglion. The lateral and medial internal nasal branches of the ophthalmic nerve supply anterior part of the nasal cavity while floor and anterior end of middle turbinate supplied by the anterior dental branch of the infra orbital nerve. Sympathetic nerve supply arises from the superior cervical ganglion; it produces vasoconstriction and decreases secretions from nose. Parasympathetic supply arises from the pterygopalatine ganglion via nerve to pterygoid canal. It produces vasodilatation and increased secretion.[41]

LATERAL WALL

Lateral wall has a characteristic complex structure as a result of scrolls and projections present on it, which are convoluted to form turbinates. These projections are the superior, middle, and inferior turbinates and occasionally when present the supreme turbinate. The inferior turbinate is a separate bone, whereas middle and superior turbinates are projection from ethmoid bone. Below and lateral to roof of each of respective turbinates, superior middle and inferior meati are found.

Superior meatus occupies the posterior third of the lateral wall, the middle meatus occupies the posterior two thirds and the inferior meatus runs the whole length of the lateral wall. Between the middle turbinate and the nasal septum is the space called olfactory cleft. Posteromedial to the superior choana is the space known as sphenoethmoidal recess to which sphenoid sinus opens. The posterior ethmoidal cells open into the superior meatus. The frontal , the anterior and the middle ethmoidal air cells and the maxillary sinus open into the

middle meatus. The nasolacrimal duct opens into the anterosuperior portion of the inferior meatus at the point where the inferior choana contacts lateral wall of the nasal cavity.[41]

NASAL MUCOUS MEMBRANE

Nasal mucous membrane consists of fairly dense connective tissue. The mucous membrane is predominantly respiratory epithelium with a small area of olfactory epithelium which covers an area of about 370 mm lying partly on the nasal septum and partly on the superior and middle turbinate . Respiratory epithelium is composed of ciliated and non-ciliated pseudo stratified columnar cells, basal pluripotent stem cells, and goblet cells. Seromucinous glands found in the sub mucosa are more important in mucous production in nasal cavity than goblet cells which are numerous in sinuses. There are about 200 cilia per cell whose tips are in superficial gel layer of mucous blanket. At anterior portion of inferior and middle turbinates there can be non ciliated cuboidal cell metaplasia due to maximum contact with inspired air.[40,42]

OSTEOMEATAL COMPLEX

Neumann coined this word to describe the region comprising middle meatus with the anterior air cells. This is the most important area for normal sinus functioning and any pathology in this area will disrupt the physiology and leads to sinus dysfunction. In the middle meatus there are several important structures. Anteriorly the first landmark is a hook shaped bone called the uncinate process. Posterior to the uncinate is a groove known as hiatus semilunaris which leads to the ethmoidal infundibulum. The ethmoidal bulla is a bulge posterior to the hiatus, which is a part of anterior ethmoidal group of cells. The frontal sinus opens into the superior most aspect of the ethmoidal infundibulum called the frontonasal recess, while the

anterior ethmoidal cells open into the infundibulum. The ostium of the maxillary sinus opens posteroinferiorly in to the infundibulum.[40]

ANATOMY OF PARANASAL SINUSES

The paranasal sinuses are arranged in pairs and include two groups anterior and posterior. The former includes maxillary sinus, frontal sinus and anterior ethmoidal sinus. The posterior group comprises of posterior ethmoidal and sphenoidal sinus.[41]

MAXILLARY SINUS

It is present since birth, but attains its maximum size around 15 to 17 years of age. The roof is formed by floor of orbit, floor by roots of canine. Posteriorly, it is related to infratemporal and pterygopalatine fossa (PPF), anterolateral walls are superficial and deep to soft tissues of face, medial wall formed by nasal cavity. The maxillary ostium present at the upper part of sinus, drains into the middle meatus. An accessory ostium is present in some people posterior to the main ostium.[40,41]

FRONTAL SINUS

It is rudimentary at birth, being represented by a small upward prolongation from anterior end of middle meatus, the nasofrontal duct. It is bound anteriorly and posteriorly by the outer and inner table of frontal bone, floor by the roof of orbital cavity, medially by the septum between the two frontal sinuses. The ostium of frontal sinus is situated in its floor, drains into middle meatus.

ETHMOIDAL SINUS

It is present at birth and in adult life and they vary in number, size and shape. They are classified into anterior and posterior, depending on whether they communicate with middle or superior meatus. They are bound medially by upper half of nasal cavity, laterally by orbit, anteriorly by frontal process of maxilla and posteriorly by sphenoid bone.[41]

SPHENOID SINUS

It is present at birth. The lateral wall is related to internal carotid artery, optic nerve and the cavernous sinus, roof is related to frontal lobe, olfactory tract, optic chiasma and pituitary gland. The floor is related to pterygoid canal, medial wall is between the two sphenoid sinus. The sphenoid ostium is situated high up in the cavity of sinus.[40,41]

PHYSIOLOGY OF NOSE -

1. Olfaction – humans can detect almost 10,000 odours and discriminate between 5000.[43]
2. Immunology – nasal secretions contain immunoglobulins,enzymes like lactoferrin and lysozymes and protective proteins like complement . neutrophils and lymphocytes are also seen.[44]
3. Sensation –mediated by branches of trigeminal and glossopharyngeal nerves, have a protective role by sneezing reflex.
4. Mucociliary clearance
5. Filtration –larger particles are filtered by nasal vibrissae. Particles 30 mm – 12 mm are trapped in mucous blanket by air turbulence

6. Warming and humidification – inspired air attains upto 80% humidity before entering lungs. Effective warming is due to opposite direction of incoming blood supply.[45]
7. Nasal cycle and airflow dynamics – 70 % of total airway resistance is from upper airway.it is essential for lungs to expand optimally while allowing venous return.[42]

PHYSIOLOGY OF SINUSES

1. Air conditioning: They serve as supplementary chambers for conditioning the inspired air by heating and moistening.[40,46]
2. mucociliary clearance
3. Vocal response: They act as resonating chambers and add to quality of voice.
4. Thermal insulators: They protect the structures in orbit and cranial fossa from intra temporal variations.
5. Balance of head: It reduces the weight of the bones of face, thereby aiding in balance of head.[40,46]

MUCOCILIARY CLEARANCE:

There is a continuous film of secretion all over the mucous membranes of nasal pharyngeal and oesophageal surfaces, from vestibule of nose to stomach. This mucous film is in continuous motion throughout its extent. The rate and direction of motion varies in different regions.generalised direction is towards the nasopharynx. The highest rate is generally found in areas best protected from the force of inspired air, that is, in the inferior and middle meati and in the posterior aspect of the nasal cavity. Few physical characteristics of nasal secretion are properties of elasticity,movement with minimal amount of friction and even spread.[46]

Drainage and ventilation and two most important factors in maintenance of normal physiology of paranasal sinuses. It depends upon the amount of mucus produced, composition of mucus, effectiveness of ciliary beat, mucosal resorption, condition of ostia and ethmoidal clefts. The mucus film has two layers: an inner serous layer, called the sol phase, in which cilia beat and an outermost viscous layer, the gel phase, which is transported by the ciliary beat. This functions like a conveyor belt. Normal nasal mucus exists at a pH range of 7.5 to 7.6.[46]

Mucociliary clearance in nasal cavity can be divided into active and inactive areas (fig). extent and distribution of these areas are relatively variable according to anatomical variations.[47]

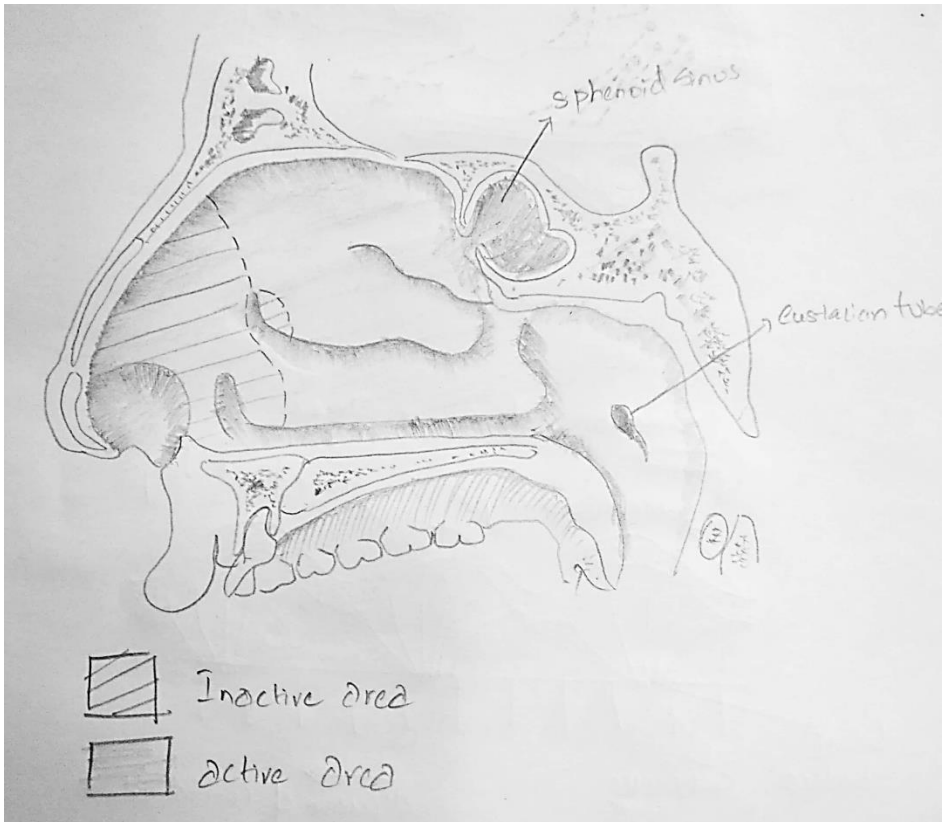


Fig 3. active and inactive areas of drainage

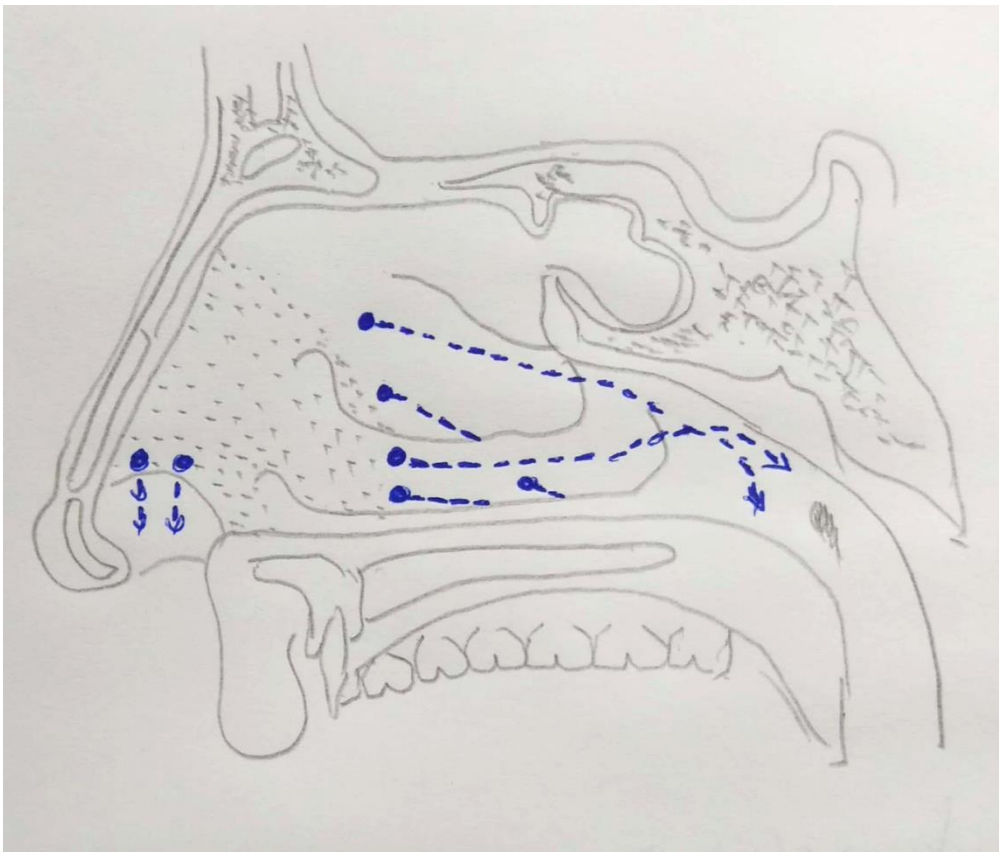


Fig 4. course of mucous in active areas

Active area-

Movement is due to the force of ciliary activity directly on the overlying mucinous secretion The rôle of gravity is negligible.

Inactive area-

Drainage of these areas is slow, and is achieved by traction on the threads of mucin in the secretion ; that is, the secretion on the inactive membrane is dragged by ciliary movement on the adjacent active membrane.[47]

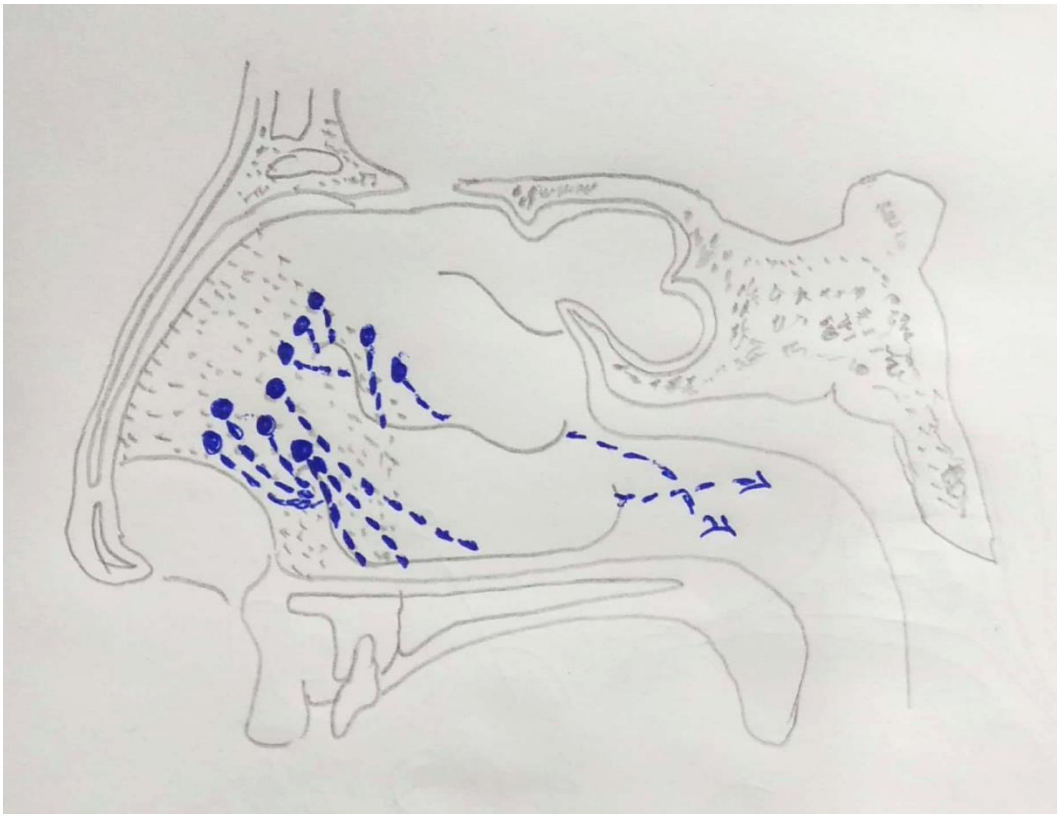


Fig 5. the course of flow of mucous on the lateral wall of nose in the inactive areas

In maxillary sinus secretion transport starts from the floor of sinus in a stellate pattern. The mucus from anterior, medial, posterior, lateral wall and roof of sinus converge at the natural ostium. This is finally drained into middle meatus.[46]

The ciliary movement of the maxillary sinus was observed to start at the bottom of the sinus and then progress upward along the antero posterior, lateral wall in the direction of the ostium leading from the sinus to the nasal cavity.

Hilding has shown in his landmark study that mucociliary clearance in maxillary sinus is towards its natural ostium. Even in the presence of accessory ostia or an inferior meatal antrostomy secretions always exited through natural ostium of maxillary sinus. If copius

amount of sectretions were present they would come out through inferior meatal antrostomy due to gravity.[47]

Mucous composition-

- Water- 97%
- Mucins-1%
- Salt-1%
- Other proteins-1%

The major macromolecular contents of mucous layer are the mucin proteins. Mucin proteins are encoded by MUC gene.[48,49]

The state of hydration is principally regulated by

- Cystic fibrosis transmemberane conductance regulator (CFTR) – controls export of chloride.
- Epithelial sodium channel (ENaC)- influx of sodium
- Calcium ion activated chloride channel (CaCC)- chloride efflux.

By regulating chloride efflux and sodium influx the epithelium controls water balance on mucosal surface.[50]

Ultrastucture of cilia-

Fawcett and Porter in 1954 have first described the characteristic ultrastructural details of cilia. Cilia are specialized organelles present in our respiratory tract.

They help in transportation of foreign materials towards oral cavity where they can be swallowed or expectorated.

Chlamydomonas as a model has helped us to understand the ultrastructure and function of cilia. The importance of cilia in maintaining airway clearance have been understood through

clinical and pathological studies of acquired and genetic forms of chronic airway diseases. Primary ciliary dyskinesia is a pathological entity which has been a research model in the field of studying mucociliary clearance.

Typical cilium is 6.5mm to 7mm long and 0.1mm in diameter.[51] Cilia's core structure – the axoneme begins in the basal body which is present at the apical region of ciliated cells. This axoneme contains two central singlet microtubules surrounded by nine outer doublet microtubules.[52] The outer doublet contains A and B tubules. A-tubule contains 13 tubulin subunits and B-tubule contains 11 subunits. Doublets are interconnected to each other by a large protein complex called nexin-dynein regulatory complex (N-DRC).[53] The A-tubules has multiple attachments like inner dynein arms (IDA) , outer dynein arms (ODA) and multi subunit protein complexes.

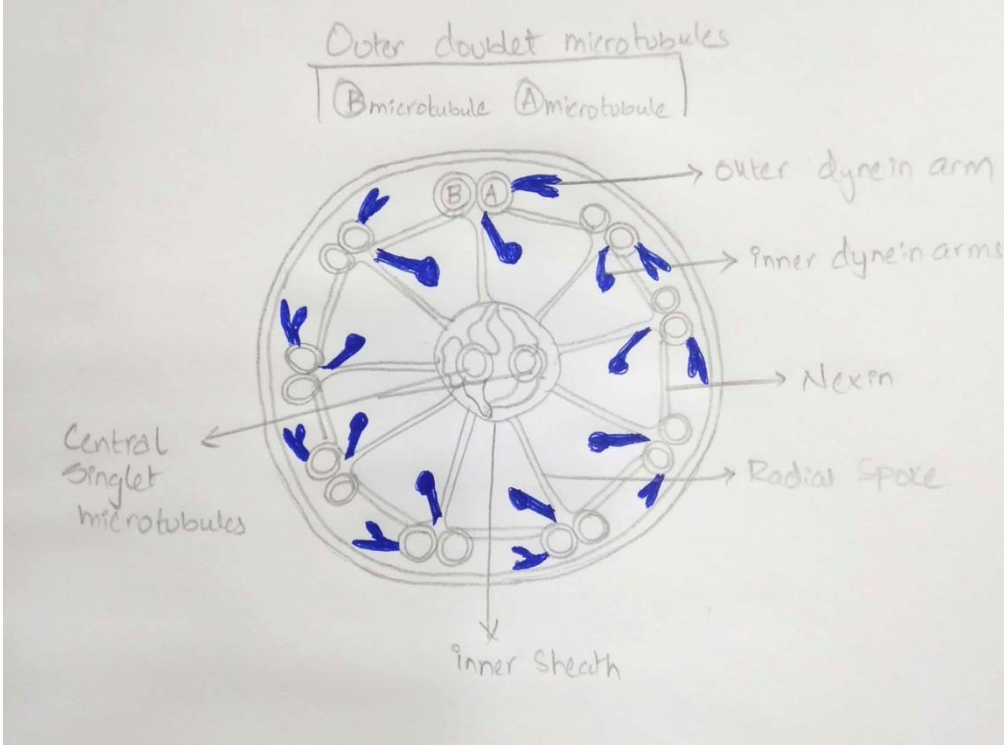


Fig 6. ultrastructure of cilia

The cilia beat in coordinated metachronal waves at a beat frequency that has multiple physiological regulators. The mechanism by which coordination establishes between adjacent cilia resulting in a metachronal wave have not yet been established. Knight –Jones have classified and described directional relationship of ciliary effective stroke and metachronal wave propagation.ATP hydrolysis provides energy for ciliary beating. Dynein arms create a mechanism such that doublet microtubules slide over each other. Controlled bending is produced by the interdoublet N-DRC and radial spoke central pair interactions. This gives an effective stroke and a recovery stoke in the same plane. Recent studies have proven that ODA regulates ciliary beat frequency and IDA regulates bend formation and waveform.[54]

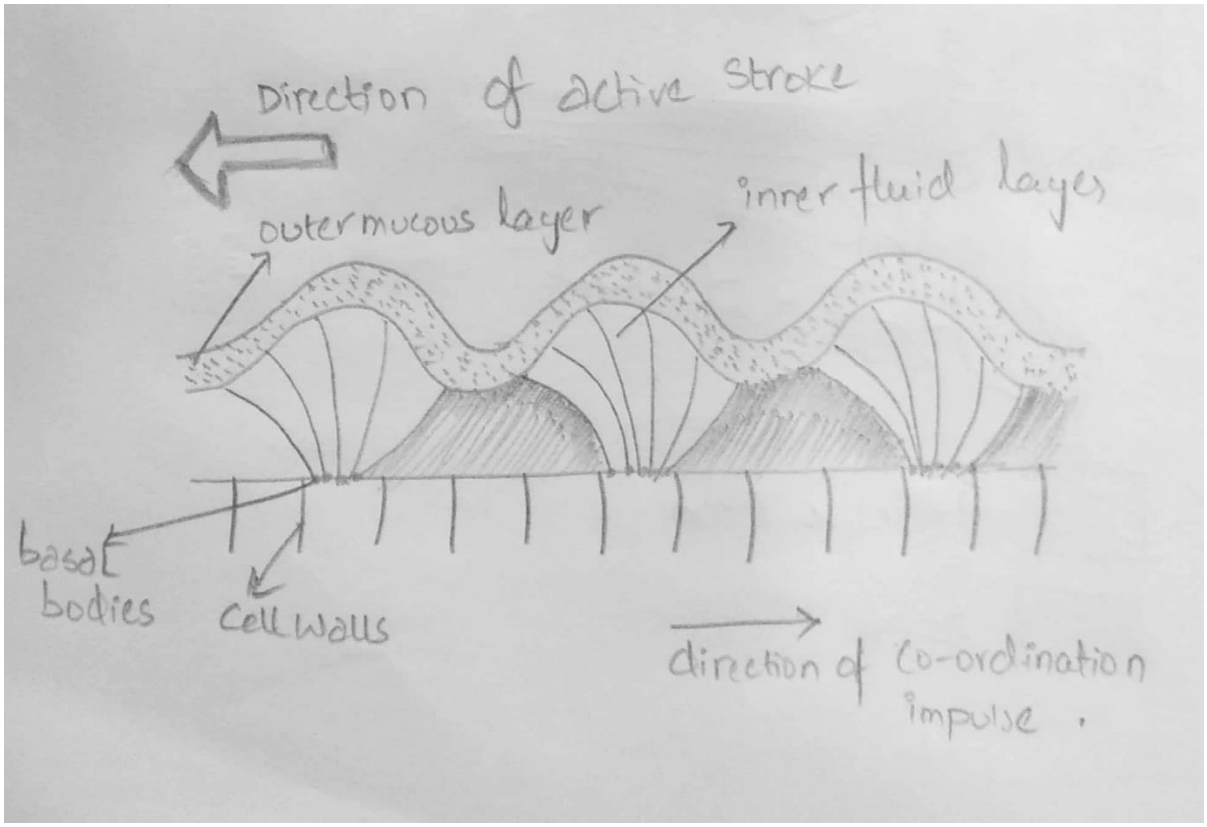


Fig 7. diagram showing mucous blanket movement and ciliary co-ordination

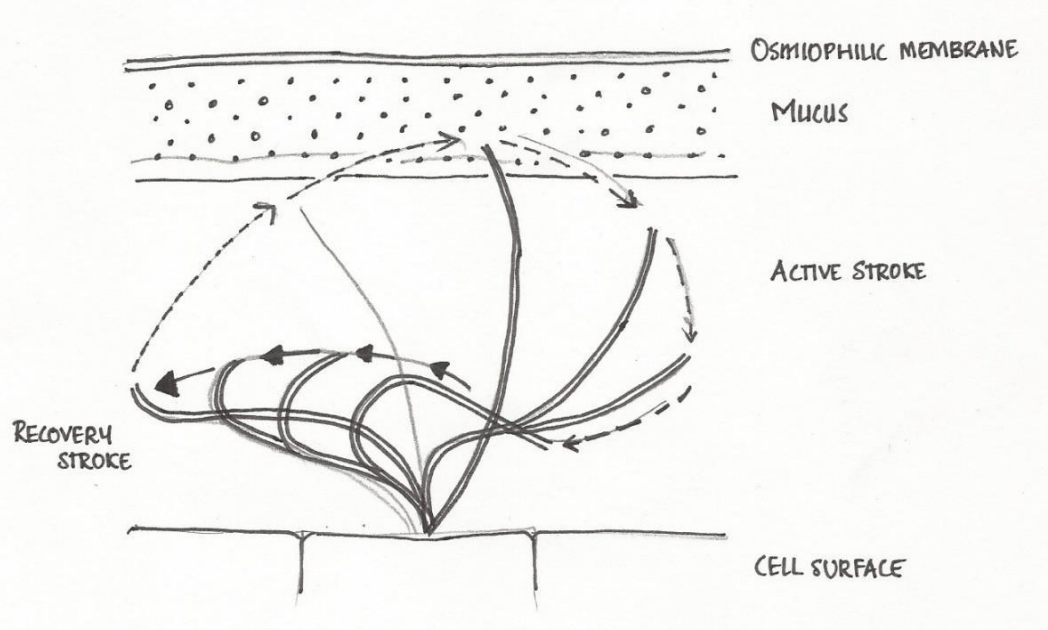


Fig 8. ciliary beat mechanism.

Measurement of mucociliary clearance of Nose and PNS

Mucociliary function can be examined by methods which are quantitative and methods which are qualitative.

Quantitative measurements-

- Mucociliary clearance
- Particle transport rate
- Angular velocity of cilia
- Ciliary beat frequency
- Mucous rheology

Qualitative measurements-

- Mucous streaming patterns
- Ciliary coordination
- Non morphometric histological studies.[55]

Transmission electron microscopy is a morphological investigation which can be performed on a single cilium level. Waveform analysis and CBF can be determined using phase contrast microscopy.[56]

The first attempts of measuring nasal mucociliary function in vivo were demonstrated by Martius in 1884 by means of stroboscopy. However, it did not attain much clinical applicability because of difficulties in handling the equipment. In 1930s and 1940s simplified analysis was attained by placing dyes in nasal cavities and observation of its appearance in oropharynx by Messerklinger, Hilding and Tremble.[57, 58]

In 1974 Anderson developed a test using food additive- sodium saccharin crystals. He placed sodium saccharine crystal along with a dye behind the head of the inferior turbinate and examiner would note the subjective finding of appreciation of sweet taste sensation by the subject or when the dye appears in oropharynx .Sodium Saccharine is a highly water soluble compound which almost immediately dissolves in nasal mucous. Normal values of nasal MCC by Anderson method are 12 to 15 minutes. These values have a greater intra or inter individual variability .Values exceeding 30 minutes are considered pathological for nasal MCC.[59] Evaluating MCC in maxillary sinus requires surgical opening. Widening the natural ostium of maxillary sinus by performing a middle meatal antrostomy can give an access to maxillary sinus floor to facilitate saccharine and dye placement. 120 minutes can be taken as pathological clearance from maxillary sinus.[60]

Because of the subjectiveness of these tests more accurate tests were developed. In 1965 proctor and wagner used I^{131} as a marker and measured its movement through nasal mucosa using gamma camera. [61]Later Harper used technicium 99m and proved to be effective. dual-label isotope method (Indium 111 and Technetium99m radiolabelled DTPA) that allowed

both the nasal cavities to be assessed simultaneously. In these radiotracer based analyses the decrease of radioactivity per unit is measured from the area involved. Results are reported in time needed for halving of radioactivity. Recently micro optical coherence tomography was also assessed in determining MCC.

FACTORS AFFECTING MCC[59]

Physical and chemical Factors

- Humidity and Temperature
- Inorganic Salts and pH
- Ionized Air and Radiations

Impairment by Inhalants

- Cigarette Smoke
- Atmospheric Pollutants
- Sulfur Dioxide
- Nitrogen Dioxide
- Ozone
- Inorganic Sulfates and Nitrates
- Oxygen
- Inhalation Anesthetics

Reduction of MCC by Pharmacologic Agents

- General Anesthetics
- Local Anesthetics
- Anticholinergic Agents

- Narcotics

Impairment in Disease States

- Nasobronchial hyper reactive states
- Cystic Fibrosis
- Respiratory Infections
- Endotracheal Intubation and Bronchoscopy
- Operative procedures (FESS, turbinate resection, etc.)
- Postoperative Retention of Secretions
- Carcinogenesis

Stimulation by Pharmacologic Agents

- Adrenergic Agents
- Cholinergic Agents
- Biologically Active Amines
- Methyl-Xanthines
- Miscellaneous Pharmacologic Agents
- Antimicrobial Drugs
- Immunopharmacologic Agents
- Corticosteroids
- Mucolytic Agents
- Cardiac Glycosides

Physical and chemical Factors

Hydration and humidification is an important aspect for maintaining normal functioning of mucociliary clearance mechanism. Changes in these parameters will in turn change the

physical properties of mucous leading to slowing down of clearance activity. Histologic changes like focal sloughing of ciliated epithelium , sub mucosal inflammation, ciliary ultrastructural changes have also been reported in areas exposed to dry air. The optimal temperature for ciliary activity is body temperature. Alkaline pH has a potential benefit on improving mucociliary transport.

Published data suggest that most oral cavity tumours are best treated with surgery, followed by adjuvant radiation with or without chemotherapy, depending on the presence of intermediate or high risk pathological features. Adjuvant radiotherapy is recommended in high-risk patients with advanced tumor, positive lymph nodes, and perineural invasion. Adjuvant concomitant chemoradiotherapy is indicated for patients with positive surgical margins and extracapsular extension.[62,63,64] One study demonstrated statistically significant mucosal thickening and Lund-Mackay scores after radiotherapy in contra lateral sinuses of patients with nasal cavity and/or paranasal sinus carcinoma.[8]

Studies have shown that radiation exposure to nasal mucosa and maxillary antrum reduces the mucociliary clearance time.[3,4,7,65,66,67,68,69] Few studies have shown significant reduction in nasal clearance time in patients receiving radiation for any head and neck tumours.[7,70,71]

MCC impairment by inhalants

Cigarette smoke causes morphologic lesions in mucosa and reduction in MCC. Long term exposure causes destruction of ciliated epithelium. Hydrogen cyanide, ammonia, formaldehyde, acrolein, and nitrogen dioxide are gas phase constituents of cigarette smoke with a depressant effect on MCC. Gaseous air pollutants like sulfur dioxide, nitrogen dioxide and ozone, and inorganic particles, sulfates and nitrates released into atmosphere through

automobile combustion all have been proven to reduce MCC. Hyperoxia has been proven to not affect clearance time while anoxia produces reversible effects. Oxygen concentration between 1-3% is sufficient to maintain normal ciliary activity. Inhalational anesthetic gases especially halothane has proven effects on MCC. Fluorochlorohydrocarbons, chromate industrial exposure are other miscellaneous agents causing impairment of particle clearance.[59]

pharmacologic agents

Studies on various pharmacologic agents suggest that general anesthetics, local anaesthetics, anticholinergic agents, narcotics and chemotherapy agents cause reduced MCC.[59,72] On the contrary adrenergic, cholinergic agents , corticosteroids, mucolytic agents, cardiac glycosides and immunopharmocologic agents have been proven to stimulate MCC.[59]

RADIOTHERAPY

Radiobiology

It is a branch of science that deals with the action of ionizing radiation on biological tissues and living organisms, is a combination of two disciplines: radiation physics and biology.

Cells contain inorganic compounds (water and minerals) as well as organic compounds (proteins, carbohydrates, nucleic acids, lipids). The two main constituents of a cell are the cytoplasm, which wires all metabolic functions within the cell, and the nucleus, which contains the genetic information (DNA). Human cells are either somatic cells or germ cells. Cells proliferate through division; division of somatic cells is called mitosis, division of germ cells meiosis. When a somatic cell divides, two cells are produced, each carrying a

chromosome complement identical to that of the original cell. The new cells themselves may undergo further division and the process continues.[74,75,76]

Somatic cells are classified as: -

- Stem cells: exist to self-perpetuate and produce cells for a differentiated cell population (e.g., stem cells of the hematopoietic system, epidermis, mucosal lining of the intestine).
- Transit cells: cells in movement to another population (e.g., a reticulocyte which is differentiating to become an erythrocyte).
- Mature cells: cells that are fully differentiated and do not exhibit mitotic activity (e.g., muscle cells, nervous tissue)

linear energy transfer (LET) is the parameter useful in defining the quality of ionizing radiation. LET focuses attention on the linear rate of energy absorption by the absorbing medium as the charged particle traverses the medium. The International Commission on Radiological Units and Measurements (ICRU) defines the LET as follows: "LET of charged particles in a medium is the quotient dE/dl, where dE is the average energy locally imparted to the medium by a charged particle of specified energy in traversing a distance of dl".[74,75,76]

Typical LET values for commonly used radiations are:

- 250 kVp x ray : 2 keV /µ m
- cobalt-60 gamma ray : 0.3 keV/µ m
- 3 MeV x ray : 0.3 keV/µ m
- 1 MeV electron : 0.25 keV/µ m

When directly ionizing radiation is absorbed in biological material, the damage to the cell may occur in one of two ways: direct or indirect action.

In direct action the radiation interacts directly with the critical target in the cell. The atoms of the target itself may be ionized or excited through Coulomb interactions leading to the chain of physical and chemical events that eventually produce the biological damage. Direct action is the dominant process in interaction of high LET particles with biological materials.[74,75,76]

In indirect action the radiation interacts with other molecules and atoms (mainly water, since 80% of a cell is composed of water) within the cell to produce free radicals that can, through diffusion in the cell, damage the critical target within the cell. In interactions of radiation with water brief yet exceedingly reactive free radicals such as H2O+ (water ion) and OH• (hydroxyl radical) are produced. The free radicals in turn can source damage to the target within the cell.[74,75,76]

The free radicals that shatter the chemical bonds and produce chemical changes that direct to biological damage are extremely reactive molecules because they have an unpaired valence electron. About two thirds of the biological damage by low LET radiations (sparsely ionizing radiation), such as x-rays or electrons, is due to indirect action. The indirect action can be altered by chemical sensitisers or radiation protectors.[74,75,76]

For the indirect action of x-rays the steps implicated in producing biological damage are as follows:

Step 1: Primary photon interaction (photoelectric effect, Compton Effect, pair production) produce one high energy electron.

Step 2: That high-energy electron in moving through tissue produces free radicals in water.

Step 3: Those free radicals may produce changes in DNA from breakage of chemical bonds.

Step 4: Those changes in chemical bonds result in biological effects.

Irradiation of a cell will result in one of the subsequent four possible outcomes:

(1) zero effect

(2) Division delay

(3) Apoptosis: the cell dies before it can divide or later by fragmentation into smaller bodies which are taken up by neighbouring cells.

(4) Reproductive failure: cell dies when attempting the first or subsequent mitosis.

The detrimental effects of radiation may be classified into two general categories: stochastic and deterministic (non-stochastic). The National Council on Radiation Protection & Measurements defines these effects as follows:

- stochastic effects are the one in which the probability of occurrence increases with increasing dose but the severity in affected individuals does not depend on the dose (induction of cancer, i.e., radiation carcinogenesis, genetic effects). There is no threshold dose for effects that are rightly stochastic.
- deterministic (non-stochastic) effects are the one which increases in severity with escalating dose, usually above a threshold dose, in affected individuals (organ atrophy, fibrosis, lens opacification, blood changes, decrease in sperm count).[74,75,76]

Early Complications

- Radiation sickness (anorexia and nausea).
- Dryness of mucous membranes (xerostomia).

- Mucositis (ulcers in mouth and pharynx).
- Skin reactions are erythema, dry and wet desquamation of skin (Fig.).
- Pharyngeal edema.
- Laryngeal edema (stridor).
- Fungal infections: Candida.
- Hematopoietic suppression.

Late Complications

- Permanent xerostomia (Dryness of mouth)
- Atrophy of skin and subcutaneous fibrosis
- Osteoradionecrosis
- Teeth decay .
- Trismus due to fibrosis of temporomandibular joint and muscles
- Transverse myelitis
- Endocrinal deficit: Thyroid and pituitary
- Eye: Retinopathy and cataract

Patient Care during Radiotherapy:

- Nutrition: Diet should be rich in protein, vitamins and iron. Nasogastric tube feeding is started if required. Blood transfusion should be given if patient has severe anemia.
- Teeth care: Dental evaluation and extraction if needed are of paramount importance and avoid osteoradionecrosis of mandible. Wound of extraction should heal before the beginning of radiotherapy. Xerostomia facilitates caries of teeth.
- Skin care: Skin reactions were common with old superficial and orthovoltage X-ray machines. The modern megavoltage therapy machine has a skin sparing effect. It is

advised to patients during radiotherapy, to: Keep the skin dry and avoid soap, water and wet shaving. Avoid sunlight. Avoid abrasive dressing and clothing and sticky plaster for dressings, which in turn peels off the desquamated skin. Skin must be covered with soft cloth, which should offer free aeration to the skin. For moist desquamated skin, use antibiotic ointment. Topical steroid creams ease itching and pain.

- Mouth care: Dryness of mouth (xerostomia) and ulcerations (mucositis) are frequently occurring and interfere with feeding. Acute radiation mucositis usually persists for 8–12 weeks after radiation. Irradiated patients are prone to acquire candida infection, which can affect mucosa of oral cavity and pharynx. Patient is asked to keep away from alcohol, tobacco and spicy food. Irritating mouthwashes contain alcohol and should be avoided. Milk of magnesia neutralizes the acid pH and avoids caries of teeth and soothes and protects inflamed mucosa. Xylocaine viscous relieves pain and discomfort of mucositis and facilitates food intake. Oral candida is generally treated by topical application of nystatin and clotrimazole. Systemic antifungal therapy is required for the mycelia, which may lie protected beneath organic debris.

Co-60 based external beam radiation therapy (EBRT)

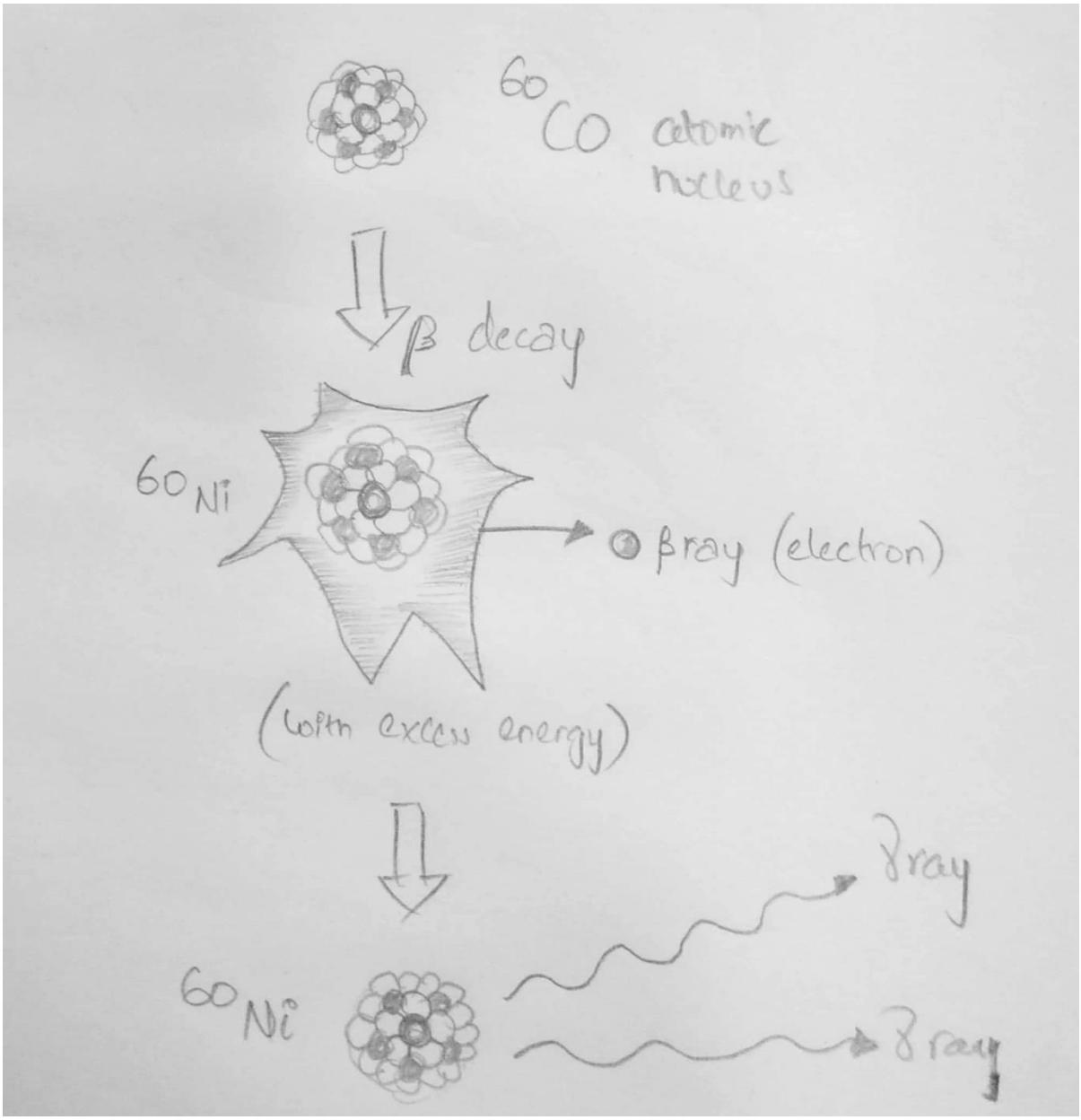


Fig 9. mechanism of Cobalt 60 emitting gamma rays

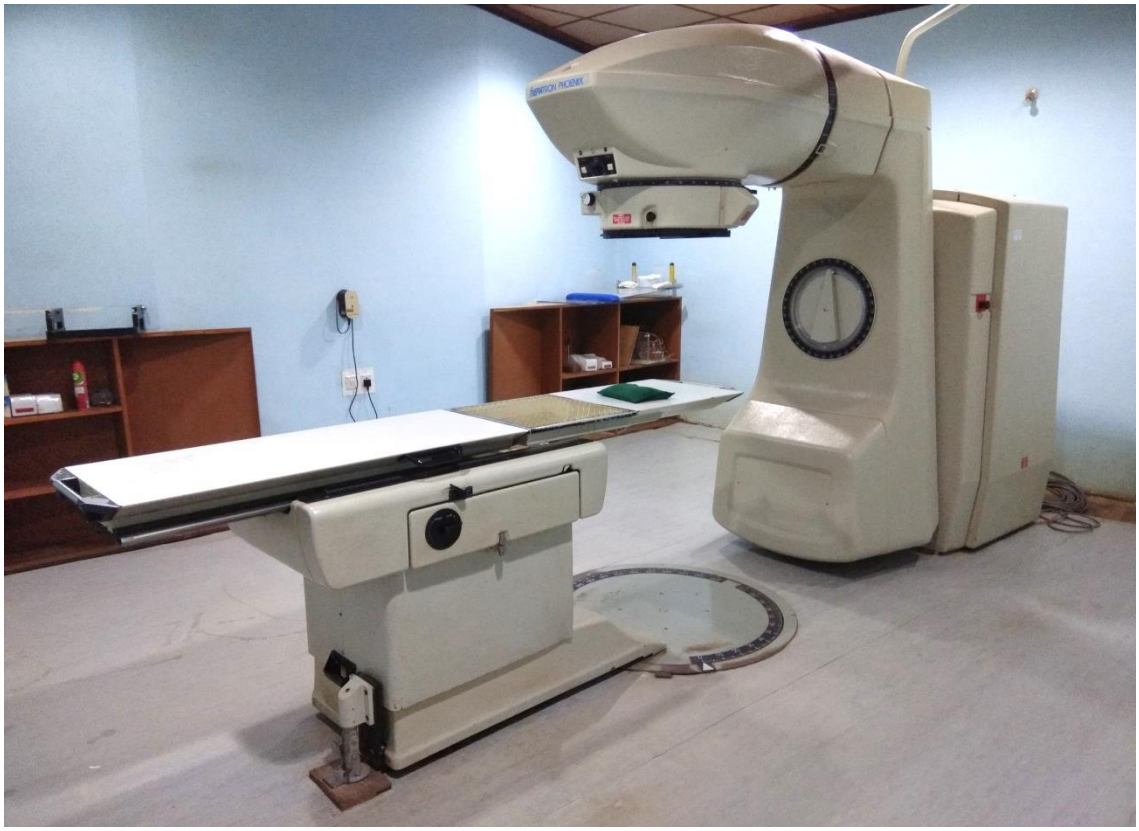


Fig 10. EBRT machine

An external sealed source of cobalt 60 (Co-60) is used in teletherapy unit as a source of gamma radiation for treatment of a variety of cancers. Co-60 produces gamma rays of a relative photon energy of 1.25MeV.With the advent of linear accelerators the usage of Co-60 teletherapy has been significantly reduced in the developed world but it is still widely used in developing nations. Few disadvantages of Co-60 machines when compared to linear accelerators are lower photon energy, lower radiation output, larger beam penumbra.

Parts of cobalt 60 machine
1. Head
2. Collimator
3. Gantry
4. Patient support assembly
5. Main frame
6. Control console

Mucociliary clearance and Radiotherapy

Direct exposure of irradiation to nasal mucosa (nasopharyngeal carcinoma, nasal and paranasal sinus carcinoma) reduces muciliary clearance and subsequently leads to development of chronic rhinosinusitis in these patients.[3,4,5,6]

An Indian study has demonstrated long term effects of radiation on MCC lasting an average duration of 5.9 years following initial treatment. Subjects who were suffering from sinusitis after radiation therapy for nasopharyngeal carcinoma were included in this study. This study also demonstrated the pathologic findings which included epithelial sloughing, ciliary loss, ciliary dysmorphism, vacoulations, collagen fibre deposition in lamina propria, epithelial metaplasia.[3]

A Japanese study observed that sloughing of ciliated cells and a decrease in total number of ciliated cells is seen within 2-3 weeks of radiation exposure. At 4 weeks , squamous metaplasia was noted and no ciliary activity was noted by 8 weeks.

In a retrospective chart review conducted in Israel on treated nasopharyngeal carcinoma patients using radiotherapy to evaluate quality of life with respect to sinonasal complications, there is fair evidence suggesting that radiation induced chronic rhinosinusitis leads to longterm quality of life impairment.[5]

CT scan evident mucosal abnormalities following radiation in nasopharyngeal carcinoma patients was also established by some studies.[65,66,67,68,69]

A south Korean study suggested that there is development of contra lateral sinus mucosal thickening when evaluated using lund mckay grading system after completion of radiation treatment for unilateral para nasal sinus malignancy.[8]

There is paucity in literature regarding effects of radiotherapy on mucociliary clearance in maxillary antra adjacent to the field of radiation. In a prospective longitudinal study conducted in Allahabad, India on 50 patients of different head and neck malignancies, it was concluded that even in absence of irradiation of nasal mucosa there were significant changes observed in mucociliary clearance. Study population included in this study were laryngeal, oropharyngeal, oral cavity and hypopharyngeal malignancies.[7]

In 2015 a study conducted in Turkey compared nasal mucociliary transport times in patients receiving radiotherapy for head and neck tumors in two different anatomic locations (nasopharyngeal carcinoma and laryngeal cancers). This showed that the effects of radiation on nasal clearance times in nasopharyngeal cancer are significantly increased during the third and sixth month of follow up. While there is demonstration of indirect effects of radiation on nasal ciliary clearance physiology in laryngeal cancer subjects in the third month of followup, recovery of function is noted during the sixth month of followup.

These studies demonstrate that nasal mucociliary clearance in patients of various head and neck cancers who underwent radiotherapy and found it to be significantly decreased irrespective to the primary site of radiation.[7,70,71]

OBJECTIVES

OBJECTIVES

1. To perform bilateral middle meatal antrostomy at the time of surgery to facilitate periodic nasal endoscopy to study and document mucosal changes in bilateral maxillary antra in patients with squamous cell carcinoma of buccal mucosa undergoing post-operative radiotherapy.
2. Compare mucociliary clearance in ipsilateral and contralateral maxillary antra in above mentioned patients.

MATERIALS AND METHODS

MATERIALS AND METHODS

SOURCE OF DATA

All patients with stage T_3,T_{4a} squamous cell carcinoma of buccal mucosa [which are diagnosed clinically and on histopathology] operated with curative intent and planned to receive postoperative radiotherapy admitted under Department of Otorhinolaryngology and Head and Neck Surgery R L JALAPPA HOSPITAL AND RESEARCH CENTRE , TAMAKA ,KOLAR during period of Dec 2015-Jul 2017.

SAMPLE SIZE

Was estimated by using the Mean Saccharine Transit Time in minutes at postoperative period in Normal Side of nasal cavity (14.7 ± 5.08) and nasal mucosa on the Side of Radiotherapy (28.86 ± 13.0) from the study done by Ko-Hsin Hu et. al., using these values at 99% Confidence limit and 99% power sample size of **24** was obtained in each category. With 10% non response sample size of 24 Normal mucosal side and 24 nasal mucosa on the Side of Radiotherapy will be included in each group.

Type of study

This study is a Prospective observational study.

$$\text{Sample size} = \frac{2SD^2(Z_{\alpha/2}+Z_{\beta})^2}{d^2}$$

SD – Standard deviation = From previous studies or pilot study

$Z_{\alpha/2} = Z_{0.05/2} = Z_{0.025} = 1.96$ (From Z table) at type 1 error of 5%

$Z_{\beta} = Z_{0.20} = 0.842$ (From Z table) at 80% power

d = effect size = difference between mean values

So now formula will be

$$\text{Sample size} = \frac{2SD^2(1.96 + 0.84)^2}{d^2}$$

$Z\,\alpha/2 = 2.58$

$Z\,\beta = 2.33$

INCLUSION CRITERIA

All patients with stages T_3,T_{4a} squamous cell carcinoma of buccal mucosa aged 18 – 70 years operated with a curative intent and planned for post-operative radiotherapy giving valid consent for bilateral middle meatal antrostomy at the time of cancer surgery and periodic endoscopy of bilateral maxillary antra.

EXCLUSION CRITERIA

1. Patients who had previously received radiotherapy in head and neck region.
2. Patients who refused post-operative radiotherapy after including in the study.
3. Patients with known causes of mucociliary dysfunction / mucositis.
4. Patients who received neoadjuvant Chemotherapy.[72]
5. Patients who were planned for post-operative chemo radiation.[72]

METHOD

Patients admitted under department of Otorhinolaryngology and Head and Neck surgery for treatment of squamous cell carcinoma of buccal mucosa were clinically evaluated and histopathologically confirmed as OSCC of buccal mucosa on biopsy. Patients presented to us in stages $T_{3,}$ T_{4a} who require composite resection and post-operative radiotherapy were selected for the study after excluding presence of confounding factors among them clinically.

The eligible patients for the study were selected and an informed consent was taken for the surgery, bilateral endoscopic middle meatal antrostomy and post operative radiotherapy after explaining all risks and complications.

Then bilateral endoscopic middle meatal antrostomy was be performed under general anaesthesia at the time of composite resection for squamous cell carcinoma.

The nasal cavities were decongested using 4% xylocaine mixed with 1 in 10,000 adrenaline soaked cotton pledgets. The aim of decongesting the nasal mucosa was

1. To make the nasal cavity room, hence facilitating endoscopic visualization
2. To reduce bleeding during the surgical procedure

The operation was performed using the endoscopic sinus surgery technique, using rigid 4 mm endoscopes (Karl-Storz, Tuttingen, Germany) with deflection angles of 0° and 30° and cold instruments.

During the procedure middle turbinate is gently medialised using a septal elevator which facilitated better visualization. Maxillary antrum was probed using an antral seeker. An incision was placed in the most anterior portion of uncinate after palpation of the junction between uncinate and lacrimal bone.

The next step was to remove the uncinate process, using a back biting forceps uncinate was cut horizontally after engaging the instrument in the ostium. Using a blakesley forceps horizontal and vertical portion of uncinate were removed completely without injuring the antral mucosa. While performing uncinectomy care was taken not to injure the mucosa over adjacent middle turbinate, because it would cause bleeding making visibility difficult.

The natural ostium of maxillary sinus was identified next. It is typically present at the level of the inferior edge of the middle turbinate, about 1/3 of the way back. This ostium was widened posteriorly and inferiorly.

This widening was done to retain the patency of ostium wide enough to perform further periodic endoscopy and tests for mucociliary clearance.

Haemostasis was achieved with nasal packing (Merocel® Medtronic Xomed Surgical Products, Jacksonville, USA) under the middle turbinate. The packing was removed on the following day by the surgeon or assistant.

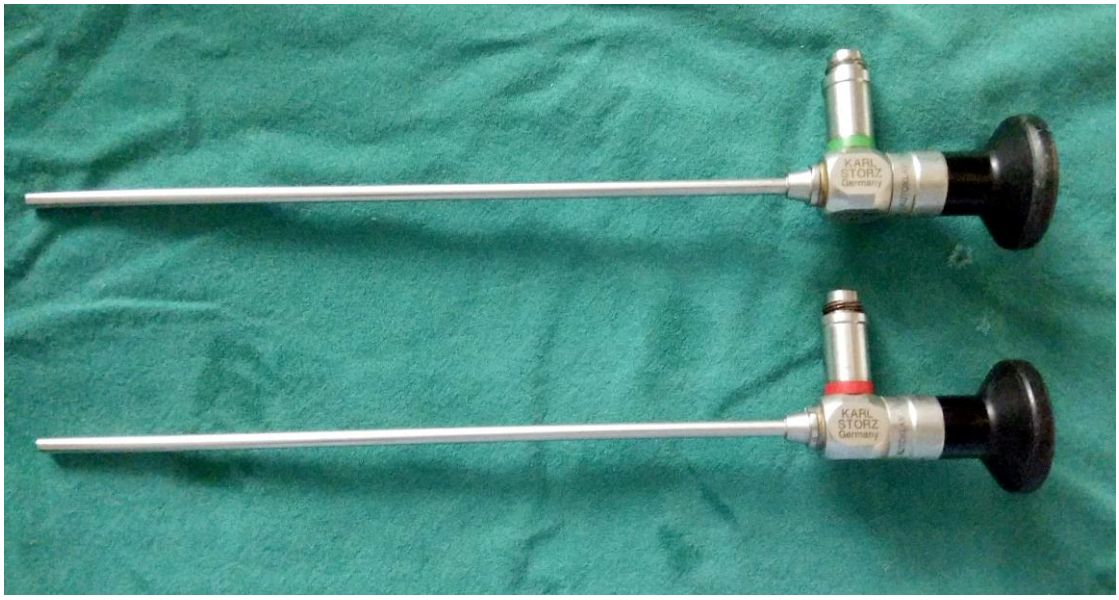


Fig 11. Rigid 4 mm endoscopes0° and 30° (Karl-Storz, Tuttingen, Germany)

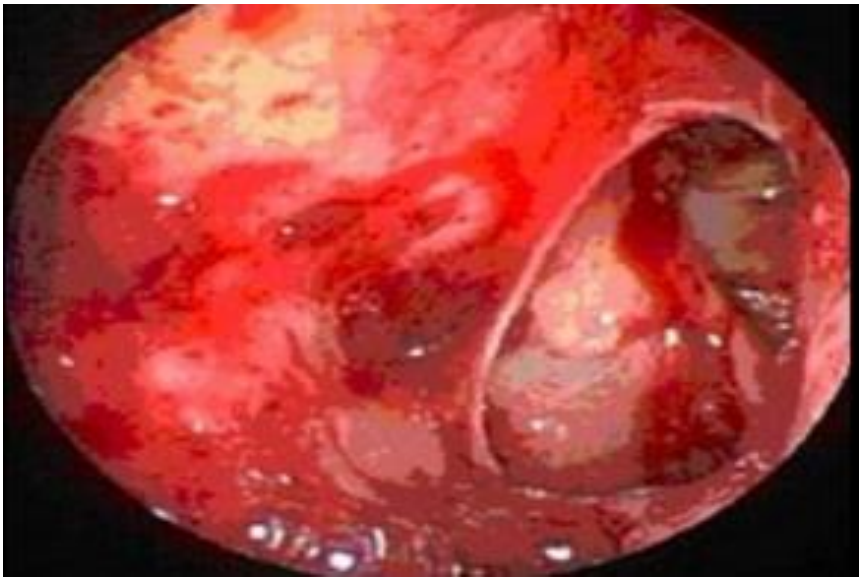


Fig 12.photograph showing middle meatal antrostomy.

Measurement of mucociliary clearance was performed using two tests

1. Methylene blue transit time (MTT)
2. Saccharine transit time (STT)

Each visit of periodic nasal endoscopy were timed at before initiating radiotherapy, each week of radiation, one and three months intervals after completion of radiotherapy.

Patient was explained about the procedure and detailed history of other radiation related complications were noted down in the proforma. Thorough saline nasal irrigation was given and nasal cavity on one side was packed with 4% xylocaine mixed with 1 in 10,000 adrenaline soaked cotton pledgets to achieve adequate vasoconstriction and make room for instrumentation.

Rigid 4 mm endoscopes (Karl-Storz, Tuttingen, Germany) with deflection angles of 0° and 30° were used to perform nasal endoscopy and the respective maxillary antra were

visualized. Using a 26 gauge spinal needle bent at its tip which was attached to a syringe a drop of 1% methylene blue aqueous dye was instilled at the junction of medial wall and floor of maxillary antrum. During this process care was taken not to touch nasal cavity mucosa. Using a heavily curved forceps a sodium saccharine crystal of $2mm^3$ (Karnataka fine chemicals, batch no.588511) was placed at the same site as the dye and the stopwatch is started.

Patient was immediately placed in sitting up position with quiet nasal breathing. During the test, patients were advised not to cough, blow nose, lean forward or backward. Patient was not allowed to drink any liquids, eat any foods during the test period.

A 30° rigid 4 mm endoscope (Karl-Storz, Tuttingen, Germany) attached to a camera, monitor and light source was used to examine the movement of dye in the maxillary antrum in 10 minute intervals. The time taken for methylene blue dye to reach the postero-inferior edge of antrostomy window is noted as MTT. 60minutes is taken as cut off for MTT. STT is measured depending on the subjective feel of taste sensation (sweet) by the patient and recorded on the stop watch. 120 minutes was considered as a cut off for STT.

Test was repeated on the opposite side after 6 hours for determining MTT and STT. Values were noted down in the patient's proforma.

Incidence and duration of other side effects of radiation like nausea, dysphagia, dysphonia, pharyngeal and laryngeal oedema, skin reactions (dry desquamation), mucositis, osteoradionecrosis and hemopoietic suppression were recorded during MCC measurements.

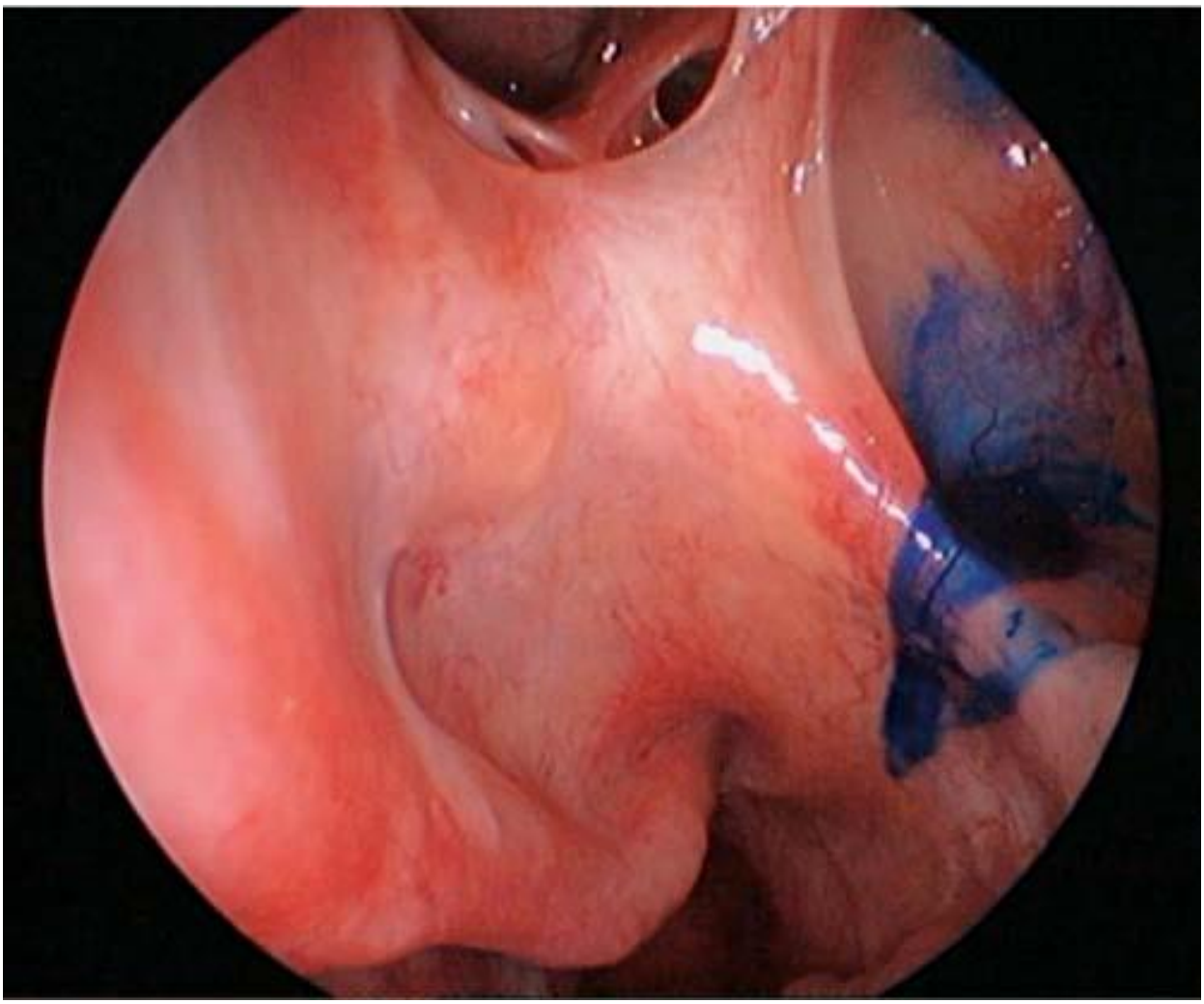


Fig 13. picture showing clearance of methylene blue dye from the maxillary antrum

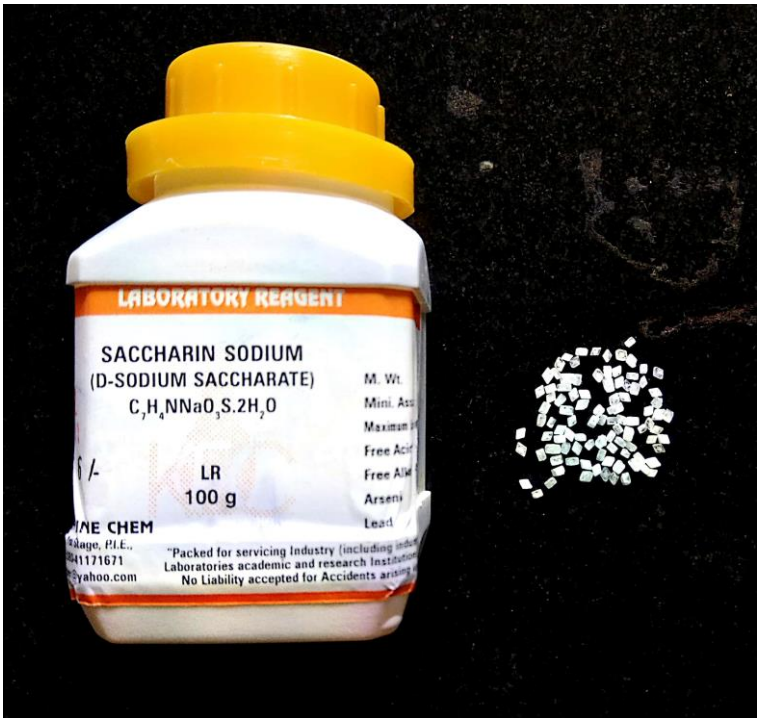


Fig 14. saccharine sodium crystals (Karnataka fine chemicals, batch no.588511)

Fig 15. picture showing size of sodium saccharine crystal 2 mm in dimension

STATISTICAL ANALYSIS

- Data was coded and entered into MS Excel data sheet and analyzed using SPSS 22 software.
- primary outcome variable: STT and MTT
- Primary explanatory variable: Radiotherapy
- Quantitative variables like saccharin and methylene blue transit times ,etc. were presented by descriptive statistics like mean and standard deviation.
- Descriptive analysis was carried out by frequency and proportion for categorical variables. Data was also represented using appropriate diagrams like bar diagram, pie diagram and box plots.
- The mean STT and MTT values at different periods were compared with base line value in both Ipsilateral and Contralateral antrum using paired t test data also represented in trend diagram.
- The STT and MTT values also compared between Ipsilateral and Contralateral maxillary antrum at base line (Pre radiotherapy) using paired t test.
- P value < 0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.
- Machines: IBM SPSS Statistics for Windows, Version 22.0. IBM Corp Armonk, NY; 2013.

OBSERVATION AND RESULTS

OBSERVATION AND RESULTS

Table 1: Descriptive analysis for Age in study population (N=24)

Parameter	Mean ±SD	Median	Min	Max	95% C.I. for EXP(B)	
					Lower	Upper
Age	47.58 ± 11.32	46.50	28.00	70.00	42.80	52.36

Median age group of sdudy population is 46.5 years old

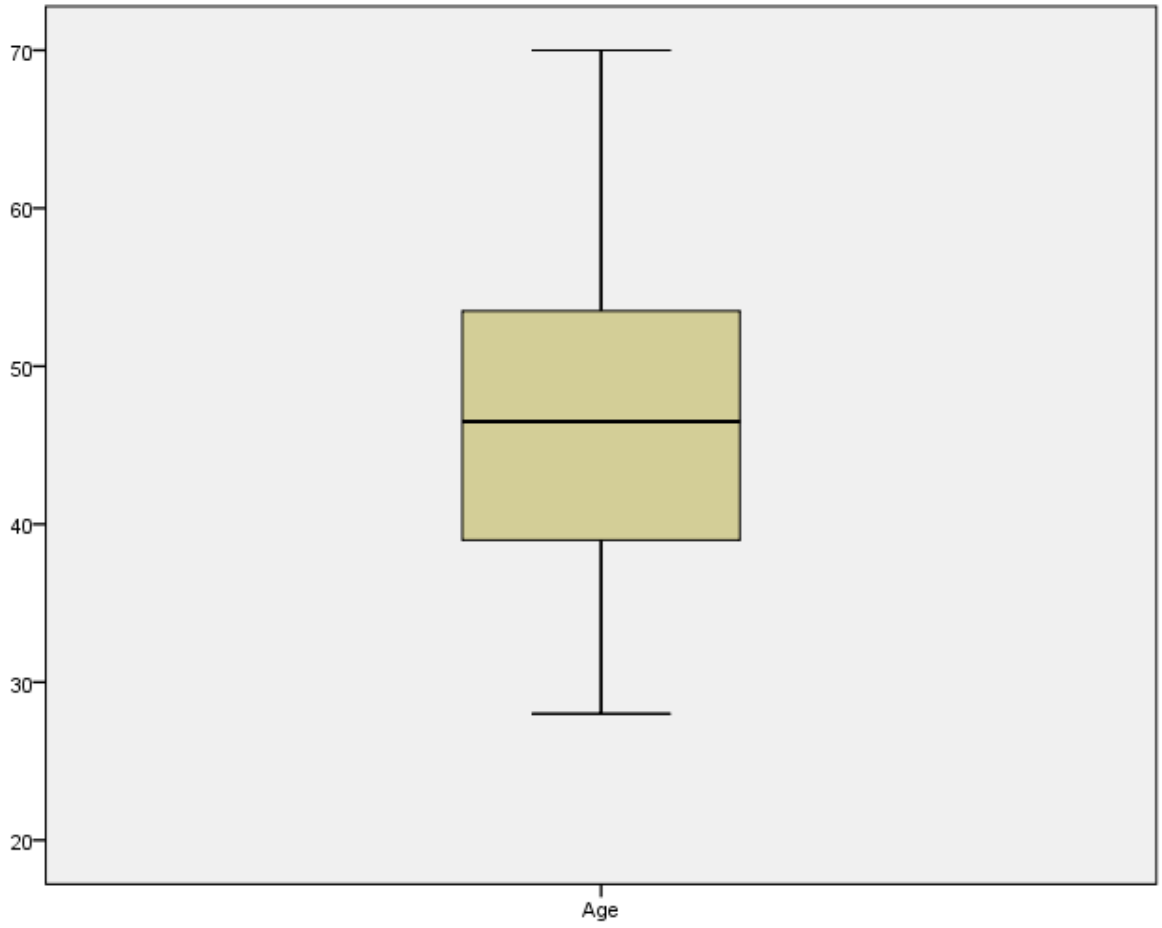


Figure 16: Box plot of age in the study population (N=24)

Table.2: Descriptive analysis of Gender in study population (N=24)

Gender	Frequency	Percentage
Female	17	70.83%
Male	7	29.17%

Majority of study population is female gender. Sex ratio male to female is 0.411

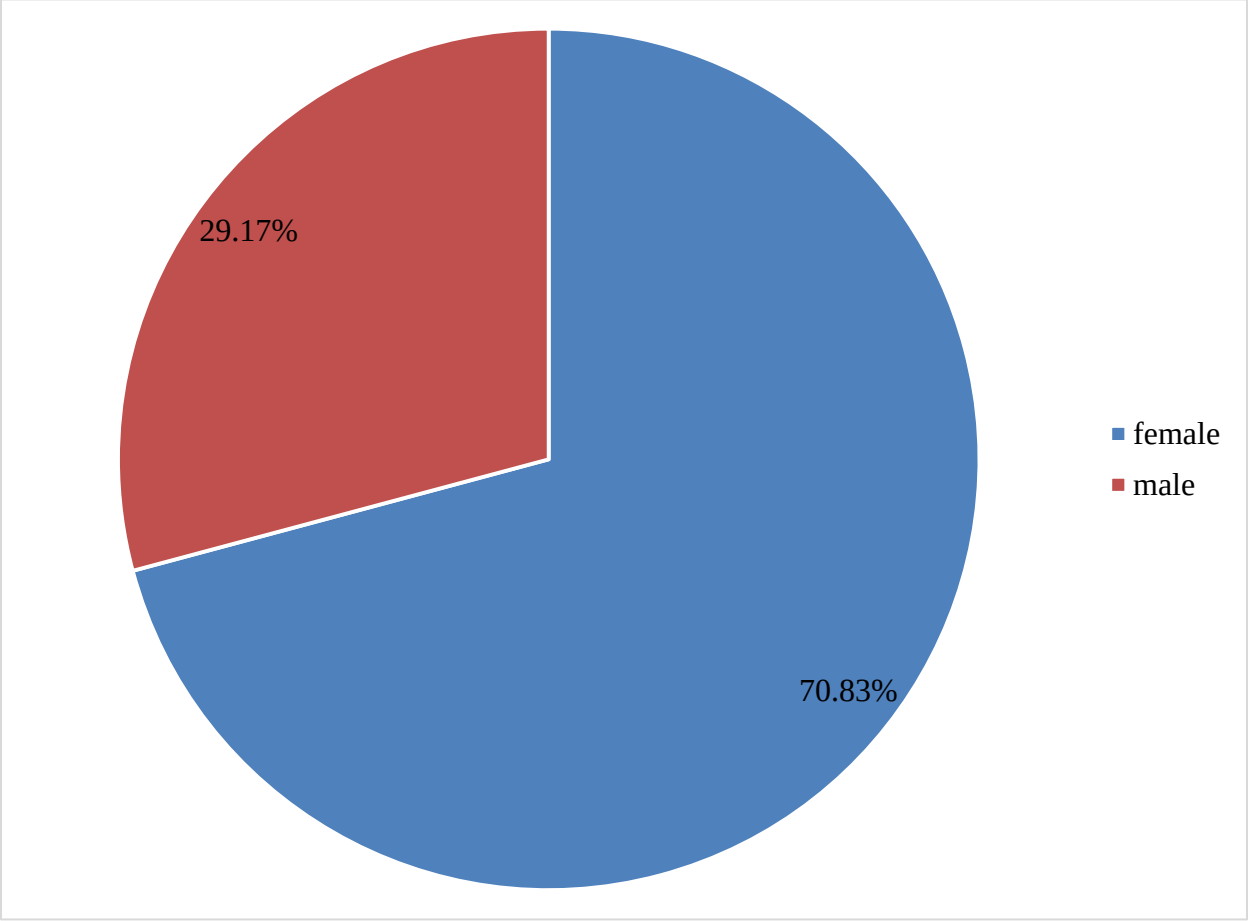


Figure 17: Pie chart of Gender distribution in study population (N=24)

Table 3. T3 and T4a lesions

TNM	Number of patients
T3	8
T4a	16

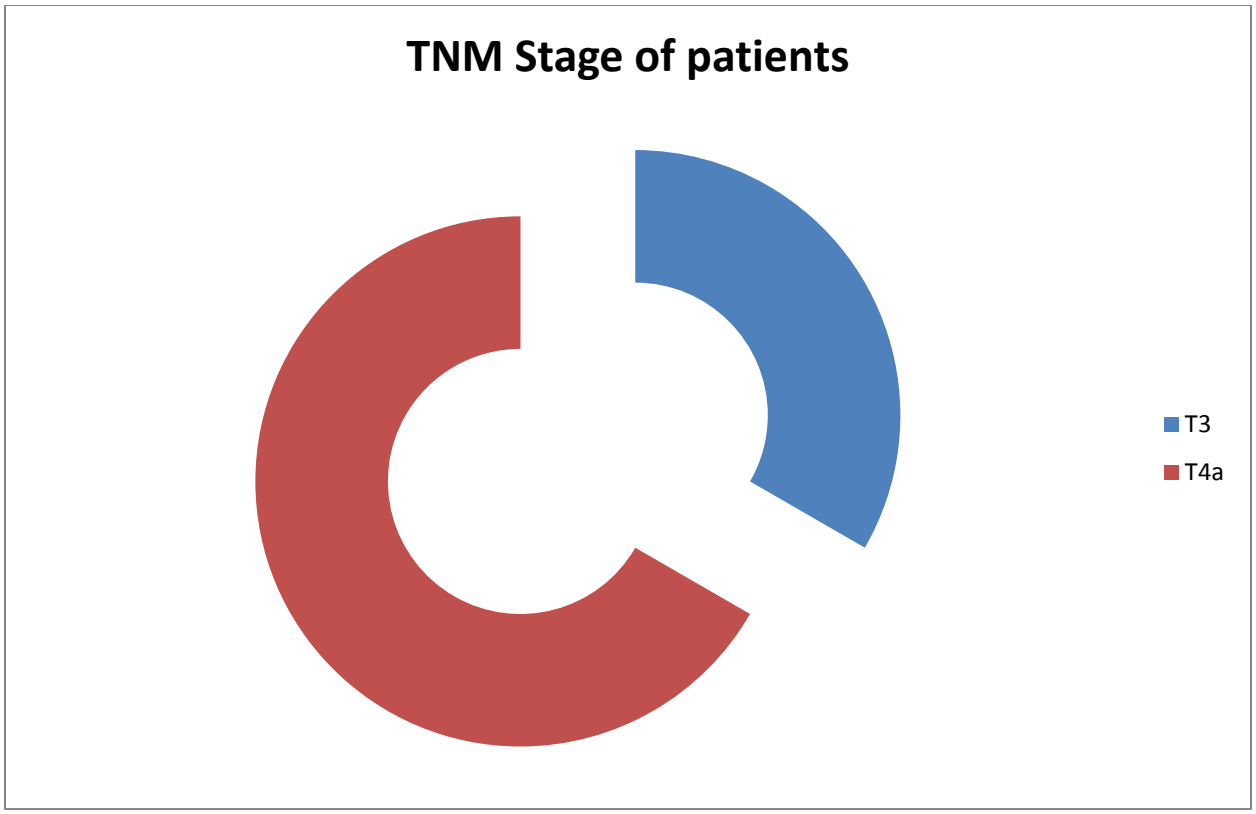


Fig 18. T3 and T4a lesions

Table.4: Trend of STT on Ipsilateral antrum (N=24):

Parameter	**Mean ± STD**	**P-value**
pre radiotherapy	45.17 ± 13.26	(Base line)
week 1	63.92 ± 21.95	***<0.001***
week 2	92.33 ± 21.8	***<0.001***
week 3	101.08 ± 18.67	***<0.001***
week 4	106.04 ± 14.72	***<0.001***
week 5	108.46 ± 12.56	***<0.001***
week 6	106.67 ± 15.73	***<0.001***
1 month post RT	100.92 ± 21.14	***<0.001***
3 month post RT	96.17 ± 22.02	***<0.001***

Table.5: Trend of MTT on Ipsilateral antrum (N=24):

Ipsilateral MTT	**Mean ± STD**	**P-value**
Pre radiotherapy	16.25 ± 6.47	(Base line)
week 1	32.08 ± 14.74	***<0.001***
week 2	50.42 ± 14.29	***<0.001***
week 3	52.5 ± 9.89	***<0.001***
week 4	52.92 ± 8.06	***<0.001***
week 5	54.17 ± 8.81	***<0.001***
week 6	56.25 ± 5.76	***<0.001***
1 month post RT	51.67 ± 10.49	***<0.001***
3 month post RT	49.58 ± 10.83	***<0.001***

Table.6: Trend of STT on Contra lateral antrum (N=24):

Parameter	Mean ± STD	P-value
pre radiotherapy	44.79 ± 16.73	(Base line)
week 1	46.17 ± 15.13	0.546
week 2	50.08 ± 18.9	0.123
week 3	49.5 ± 16.68	0.097
week 4	47.83 ± 16.54	0.221
week 5	50.38 ± 14.83	0.063
week 6	47.83 ± 14.27	0.206
1 month post RT	47.33 ± 12.1	0.407
3 month post RT	44.08 ± 12.2	0.818

Table.7: Trend of MTT on Contra lateral antrum (N=24):

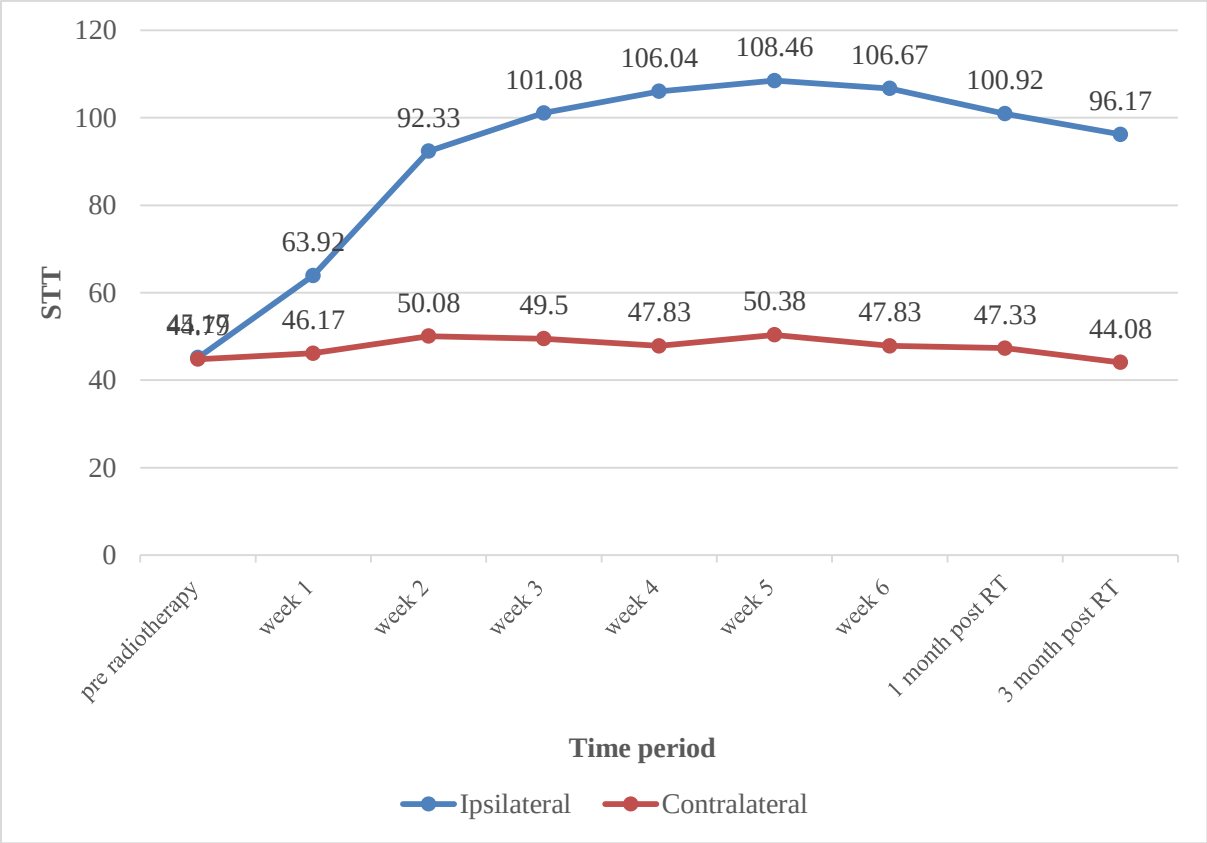
Parameter	Mean ± SD	P-value
pre radiotherapy	17.08 ± 5.5	(Base line)
week 1	20 ± 9.78	0.110
week 2	20.83 ± 8.81	0.017
week 3	21.67 ± 8.16	0.001
week 4	19.58 ± 8.06	0.083
week 5	21.25 ± 6.12	<0.001
week 6	20.42 ± 6.9	0.008
1 month post RT	20 ± 5.9	0.070
3 month post RT	19.17 ± 7.17	0.096

Table.8: Comparison of STT between Ipsilateral and Contralateral antra before and after radiotherapy (N=24)

STT	Ipsilateral Mean ± STD	Contralateral Mean ± STD	P-value
pre radiotherapy	45.17 ± 13.26	44.79 ± 16.73	0.859
week 1	63.92 ± 21.95	46.17 ± 15.13	***<0.001***
week 2	92.33 ± 21.8	50.08 ± 18.9	***<0.001***
week 3	101.08 ± 18.67	49.5 ± 16.68	***<0.001***
week 4	106.04 ± 14.72	47.83 ± 16.54	***<0.001***
week 5	108.46 ± 12.56	50.38 ± 14.83	***<0.001***
week 6	106.67 ± 15.73	47.83 ± 14.27	***<0.001***
1 month post RT	100.92 ± 21.14	47.33 ± 12.1	***<0.001***
3 month post RT	96.17 ± 22.02	44.08 ± 12.2	***<0.001***

There is a significant increase in STT on radiation side when compared to non irradiated side.

Figure.19: Trend diagram of comparison of STT between Ipsilateral and Contralateral before and after radiotherapy (N=24)



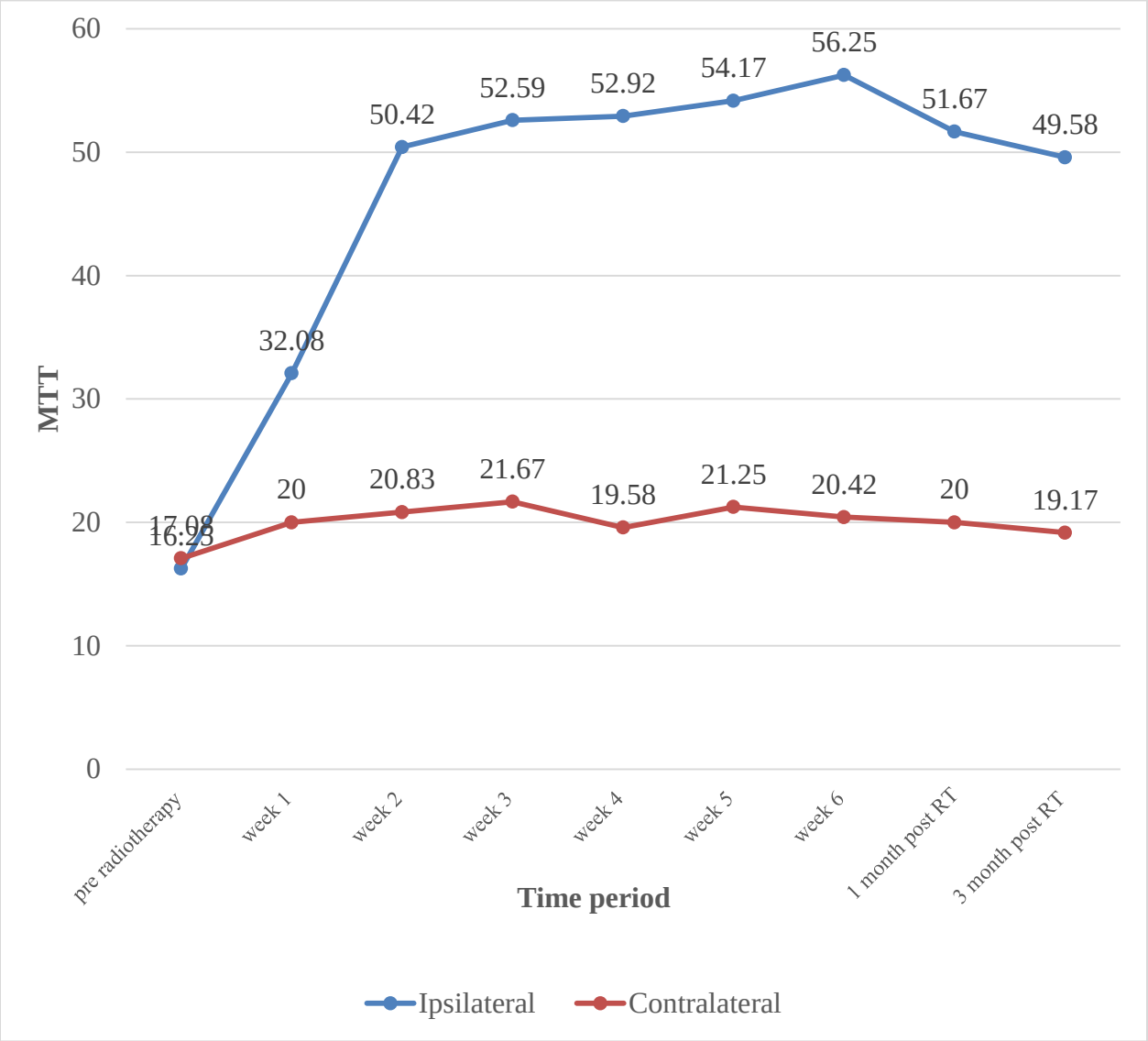
There is a significant increase in STT on radiation side when compared to non irradiated side. Trend diagram shows significant increase from 2nd week of radiation and slight improvement from 1 month after completion of treatment. However STT did not come back to its baseline pre radiation values even after 3 months of completion of treatment. The residual delay was a maximum of 63.29 minutes at week 5 of radiation and during third month of follow up it was 51 minutes showing some improvement.

Table.9: comparison of MTT between Ipsilateral and Contralateral before and after radiotherapy (N=24)

MTT	Ipsilateral Mean ± STD	Contralateral Mean ± STD	P-value
pre radiotherapy	16.25 ± 6.47	17.08 ± 5.5	0.575
week 1	32.08 ± 14.74	20 ± 9.78	***<0.001***
week 2	50.42 ± 14.29	20.83 ± 8.81	***<0.001***
week 3	52.5 ± 9.89	21.67 ± 8.16	***<0.001***
week 4	52.92 ± 8.06	19.58 ± 8.06	***<0.001***
week 5	54.17 ± 8.81	21.25 ± 6.12	***<0.001***
week 6	56.25 ± 5.76	20.42 ± 6.9	***<0.001***
1 month post RT	51.67 ± 10.49	20 ± 5.9	***<0.001***
3 month post RT	49.58 ± 10.83	19.17 ± 7.17	***<0.001***

There is a significant increase in STT on radiation side when compared to non irradiated side

Figure.20: Trend diagram of comparison of MTT between Ipsilateral and Contralateral before and after radiotherapy (N=24)



There is a significant increase in MTT on radiation side when compared to non irradiated side. Trend diagram shows significant increase from 2nd week of radiation and slight improvement from 1 month after completion of treatment. However MTT did not come back to its baseline pre radiation values even after 3 months of completion of treatment. The residual delay was a maximum of 40 minutes at week 6 (towards the end of radiation) and during third month of follow up it was 33.33 minutes showing some improvement.

Table 10: Descriptive analysis of nausea in study population (N=24)

Nausea	Frequency	Percent
nil	7	29.17%
week 2-6	5	20.83%
week 3-6	5	20.83%
week 4-6	3	12.50%
week 5-6	3	12.50%
week3-6	1	4.17%

Majority of study population had complaints of nausea throughout the period of radiotherapy

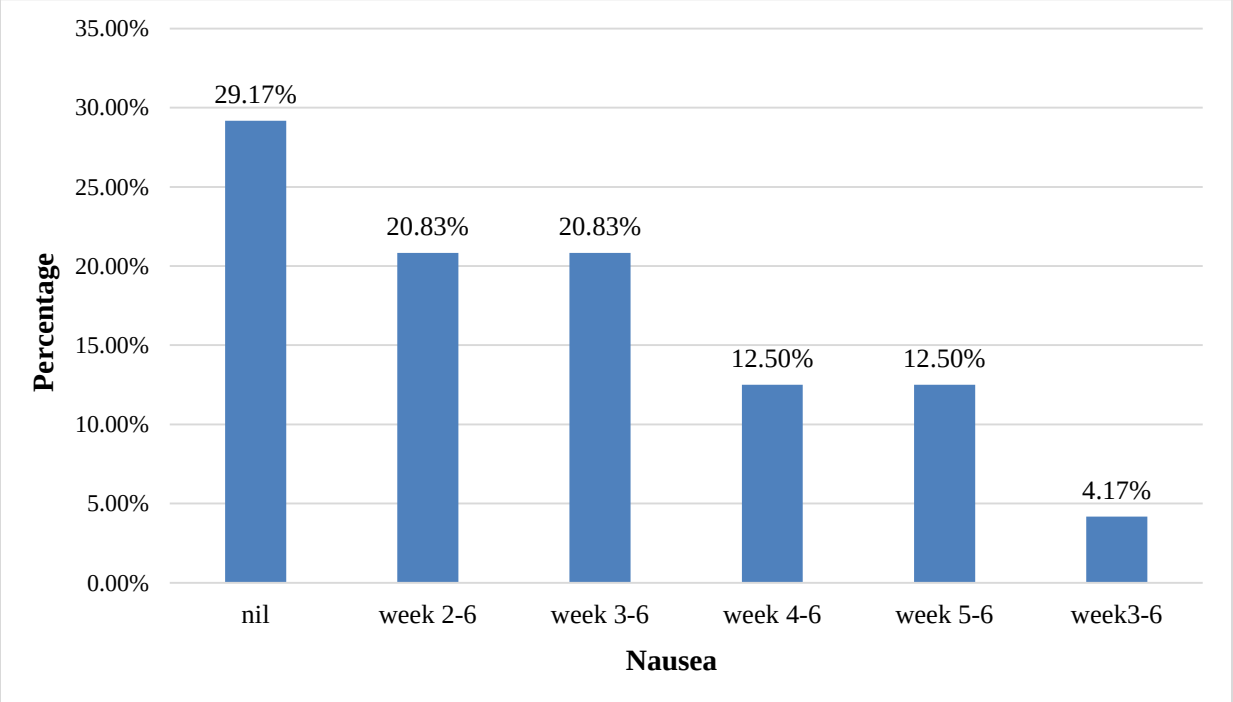


Figure 21: Bar chart of nausea in study population (N=24)

Table 11: Descriptive analysis of dysphagia in study population (N=24)

Dysphagia	Frequency	Percent
nil	4	16.67%
week 2-6	2	8.33%
week 3-6	3	12.50%
week 4-6	4	16.67%
week 5-6	5	20.83%
week 6	6	25.00%

Majority of study population had dysphagia complaints towards the end of radiation therapy.

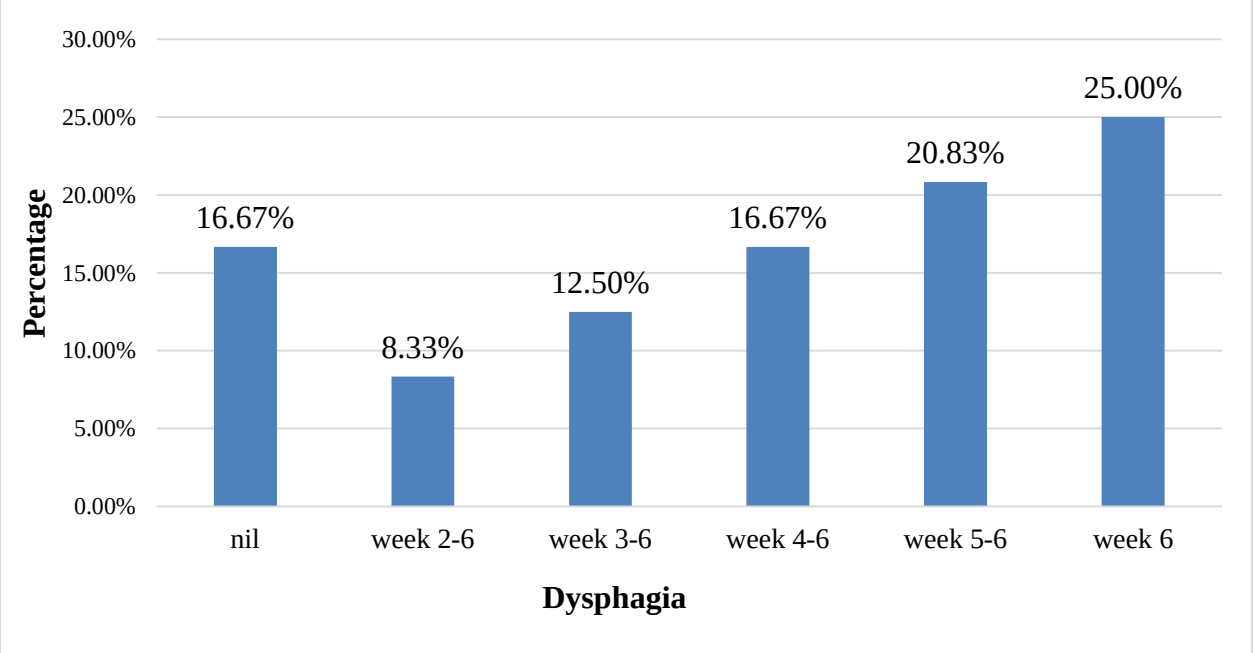


Figure 22: Bar chart of dysphagia in study population (N=24)

Table 12: Descriptive analysis of mucositis in study population (N=24)

Mucositis	Frequency	Percent
Nil	5	20.83%
week 2-6	3	12.50%
week 3-6	5	20.83%
week 4-6	4	16.67%
week 5-6	4	16.67%
week 6	3	12.50%

Majority of study population had mucositis throughout the period of radiotherapy

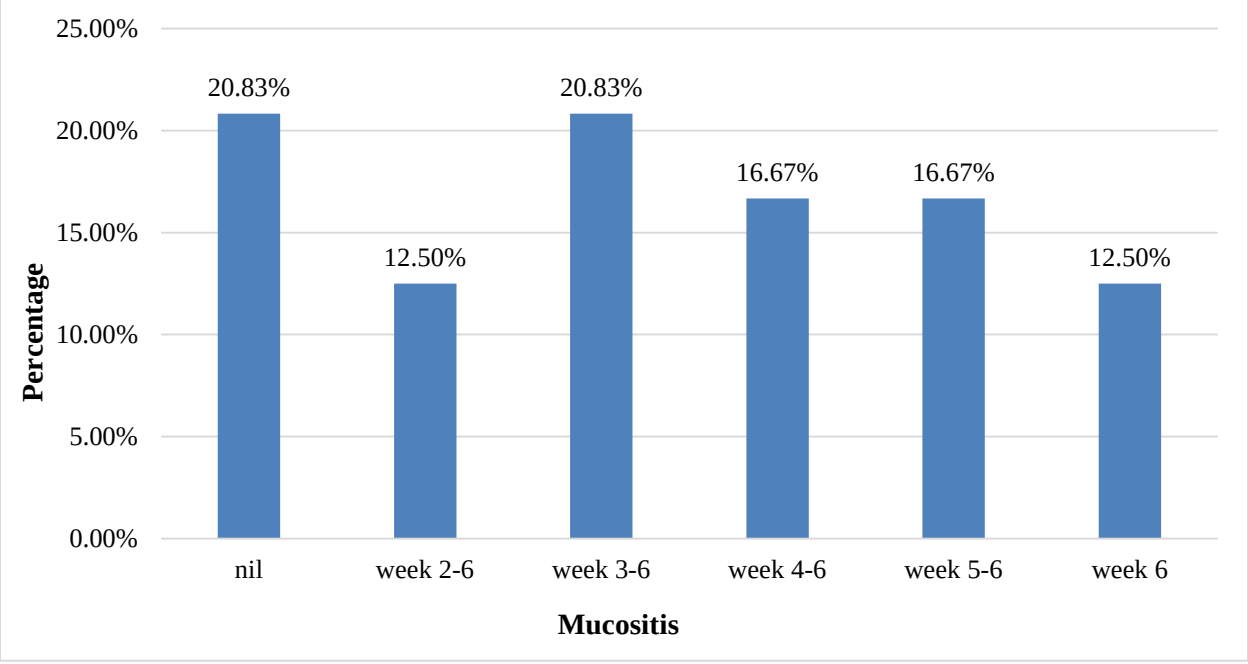


Figure 23: Bar chart of mucositis in study population (N=24)

Table 13: Descriptive analysis of skin reaction in study population (N=24)

Skin reaction (dry desquamation)	Frequency	Percentages
nil	5	20.83%
week 2-6	7	29.17%
week 3-6	3	12.50%
week 4-6	6	25.00%
week 5-6	3	12.50%

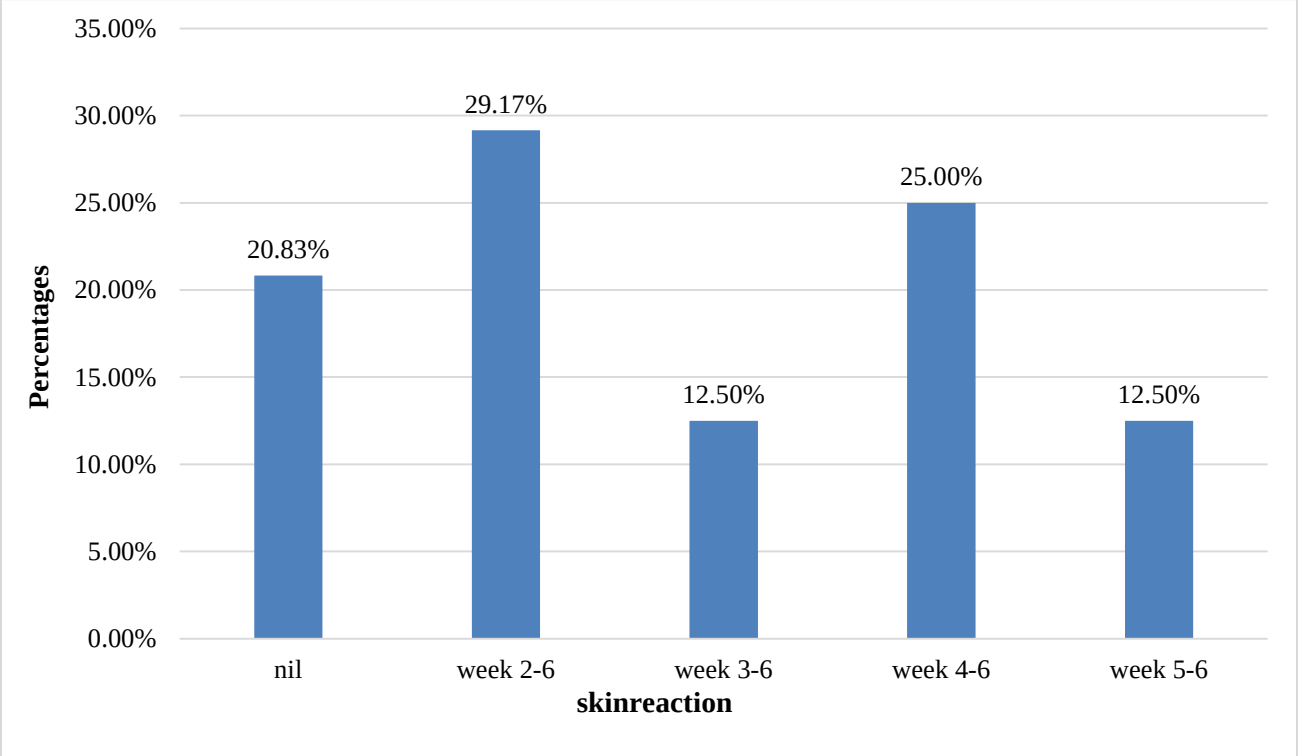


Figure 24: Bar chart of skin reaction in study population (N=24)

Table 14: Descriptive analysis of pharyngeal edema in study population (N=24)

Pharyngeal edema	Frequency	Percentages
nil	16	66.67%
week 3-6	1	4.17%
week 4-6	1	4.17%
week 5-6	1	4.17%
week 6	5	20.83%

Majority of study population did not demonstrate any signs of pharyngeal oedema

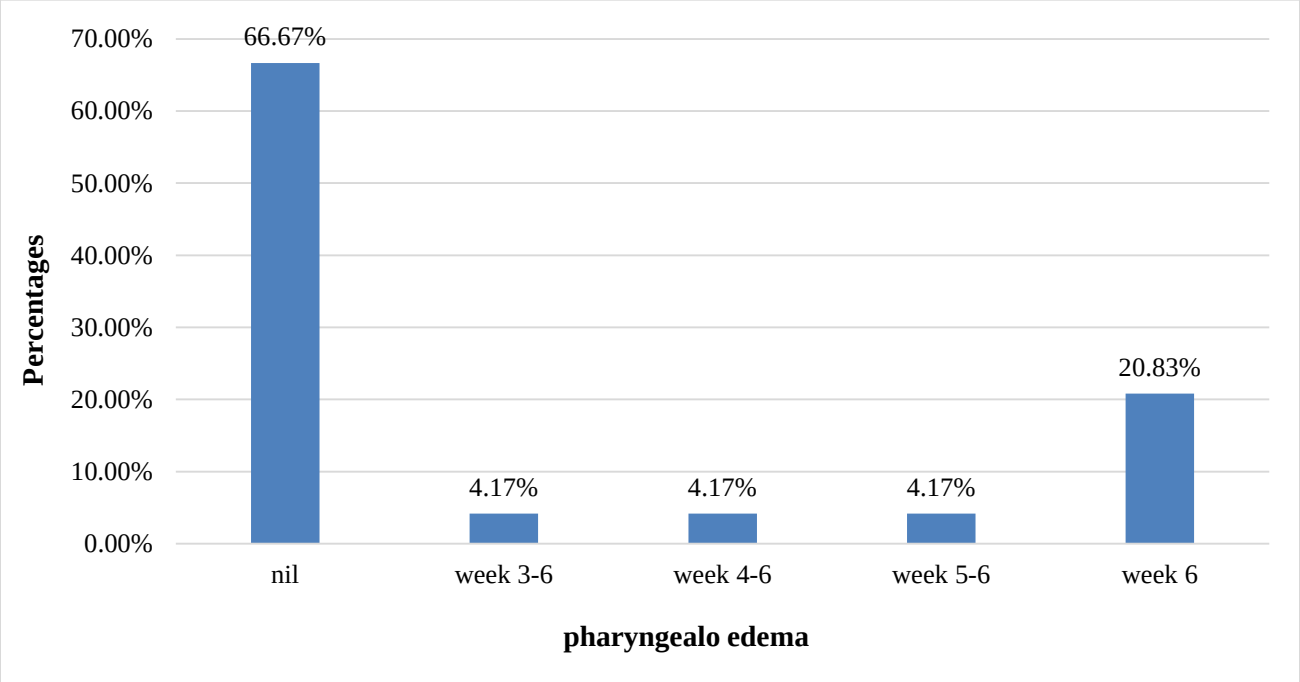


Figure 25: Bar chart of pharyngeal edema in study population (N=24)

Table 15: Descriptive analysis of fungal infection in study population (N=24)

Fungal Infection	Frequency	Percentage
Nil	23	95.83%
week 6	1	4.17%

Only one patient had oral candidiasis.

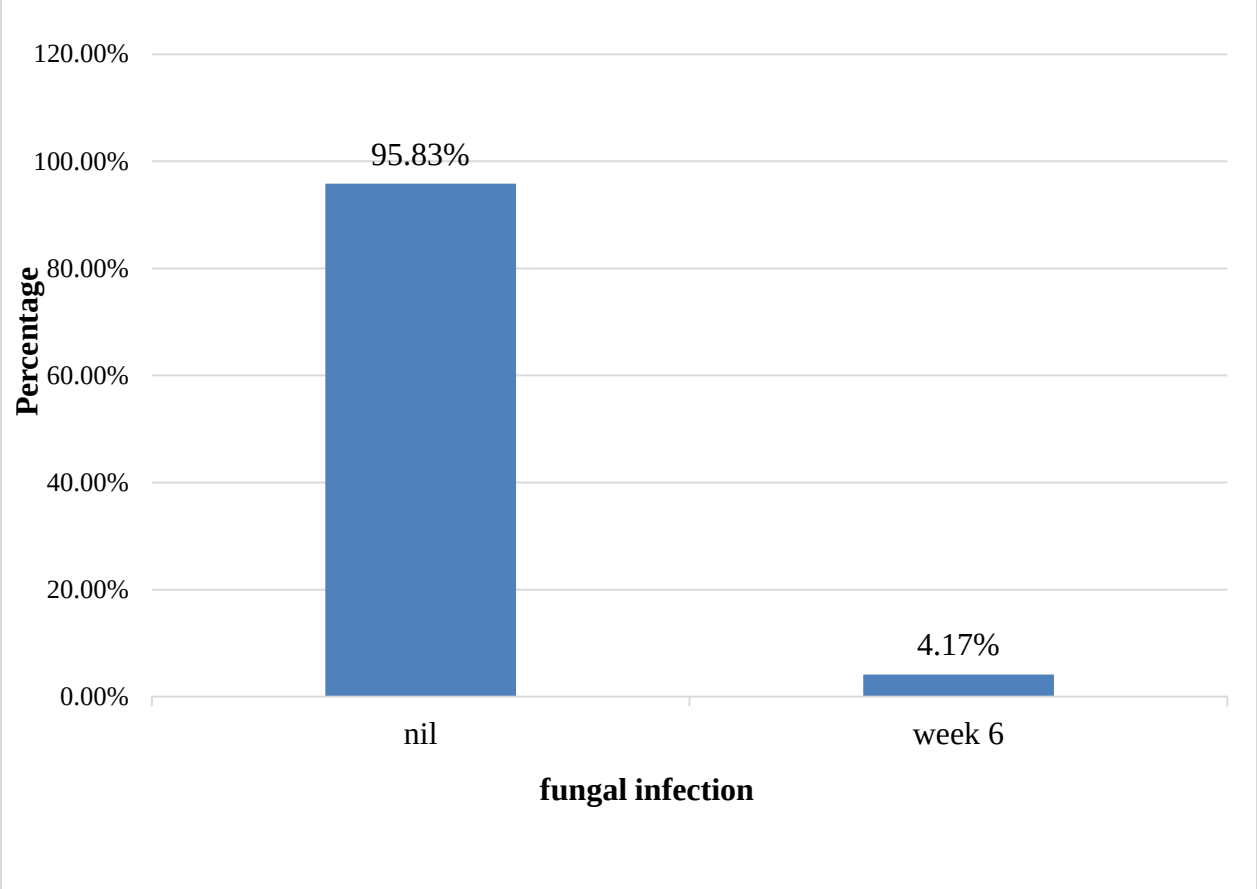


Figure 26: Bar chart of fungal infection in study population (N=24)

Table 16 : Descriptive analysis of laryngeal oedema in study population (N=24)

laryngeal oedema	Frequency	Percentage
nil	16	66.67%
week 4-6	1	4.17%
week 5-6	3	12.50%
week 6	4	16.67%

Majority of study population did not have laryngeal oedema. The patients who developed odema are during the last two weeks of radiation therapy

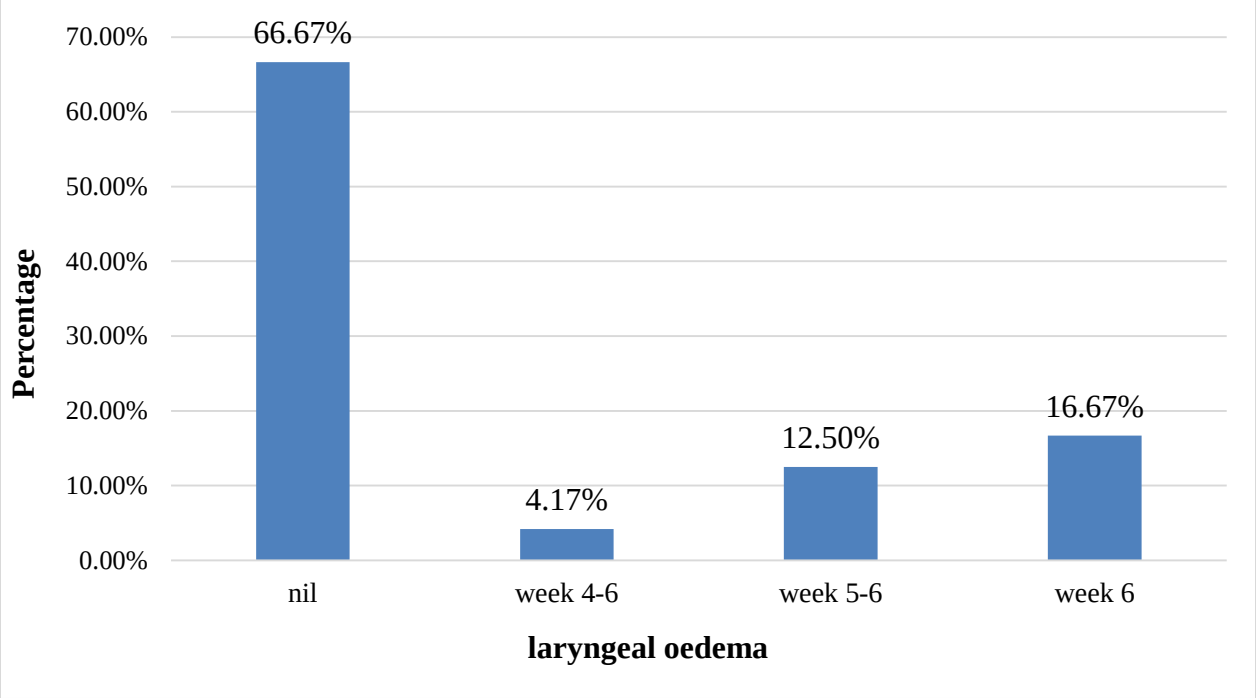


Figure 27: Bar chart of laryngeal oedema in study population (N=24)

Table 17: Descriptive analysis of dysphonia in study population (N=24)

Dysphonia	Frequency	Percentage
nil	16	66.67%
week 4-6	1	4.17%
week 5-6	2	8.33%
week 6	5	20.83%

Majority of study population did not have dysphonia. Similar to the patients who developed odema , dysphonia complaint was also observed during last two weeks of radiation therapy.

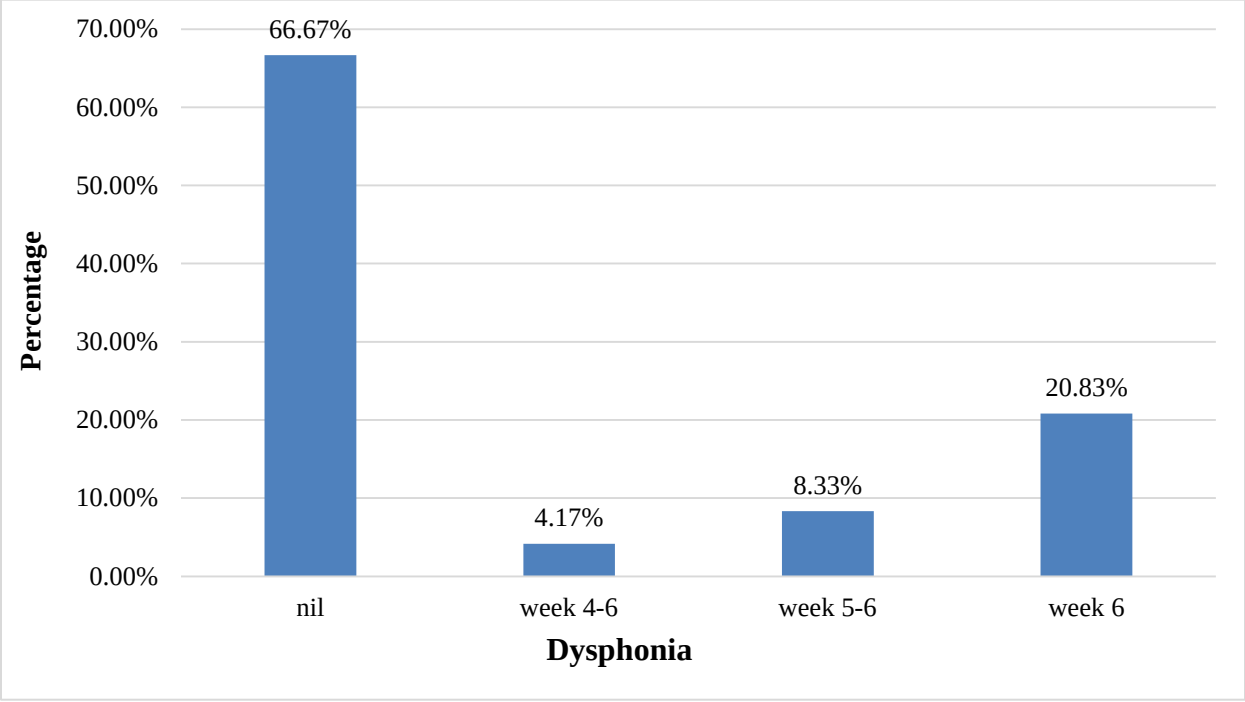


Figure 28: Bar chart of dysphonia in study population (N=24)

Table 18: Descriptive analysis of contractures in study population (N=24)

Contractures	Frequency	Percentage
3rd post radiation month	22	91.67%
Nil	2	8.33%

Majority of fibrosis and contractures in the area of radiation exposure are observed during the third post radiotherapy month

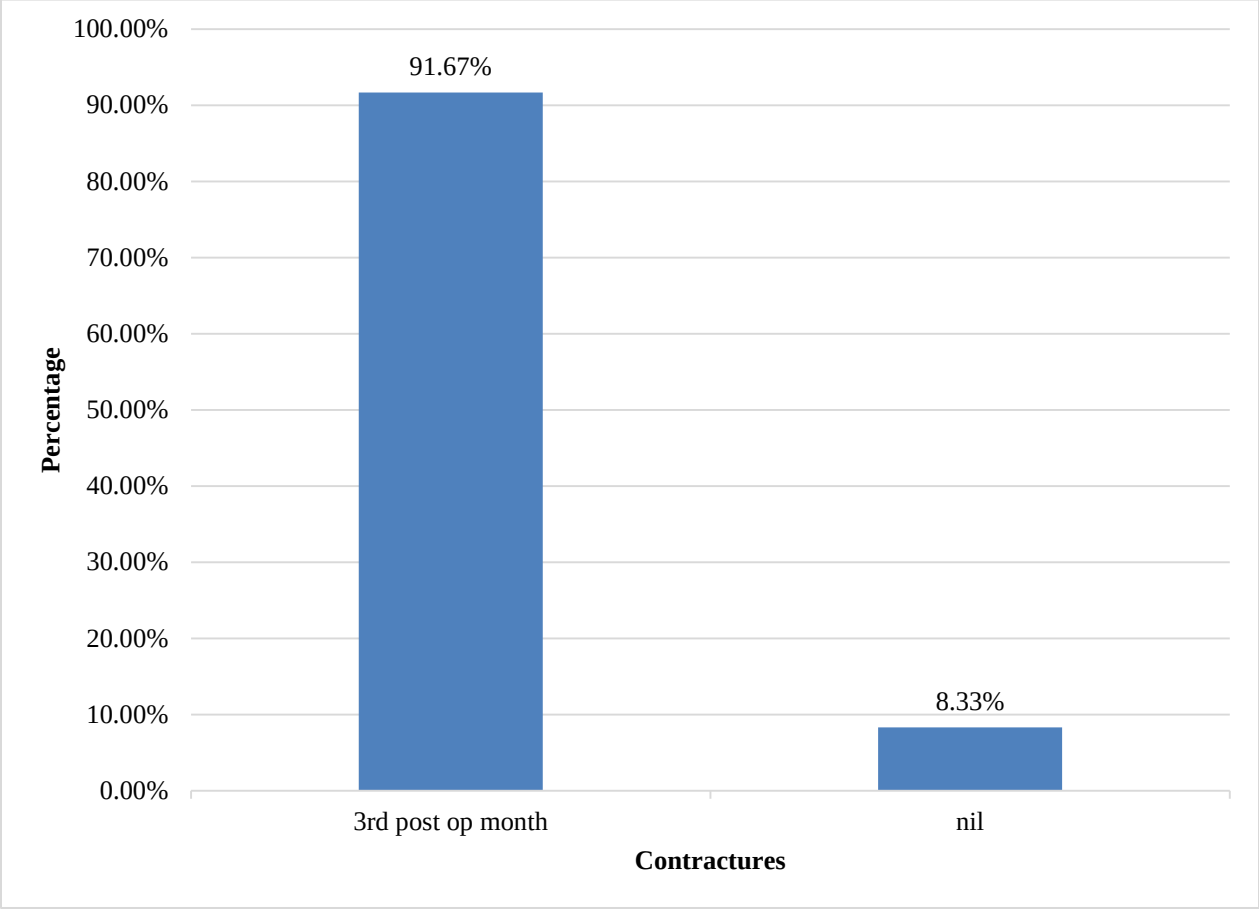


Figure 29: Bar chart of contractures in study population (N=24)

Table 19: Descriptive analysis of osteoradionecrosis in study population (N=24)

Osteoradionecrosis	Frequency	Percentage
Nil	24	100.00%

There were no subjects who developed osteoradionecrosis in the study population.

Table 20: Descriptive analysis of hematopoietic suppression in study population (N=24)

Hematopoietic suppression	Frequency	Percentage
Nil	24	100.00%

There were no subjects who developed hemopoietic suppression in the study population.

DISCUSSION

DISCUSSION

This is a study performed on patients presented with stage T_3,T_{4a} squamous cell carcinoma of buccal mucosa [who were diagnosed clinically and on histopathology] operated with curative intent and planned to receive postoperative radiotherapy admitted under Department of Otorhinolaryngology and Head and Neck Surgery R L JALAPPA HOSPITAL AND RESEARCH CENTRE , TAMAKA ,KOLAR during period of Dec 2015-Jul 2017. We performed bilateral middle meatal antrostomy at the time of surgery to facilitate periodic nasal endoscopy to evaluate MCC.

Results of our study demonstrate a female preponderance in the study subjects (male to female sex ratio was 0.411), which may be attributed to the quid chewing habit and demographic characteristics of kolar district population.

The prevalence of oral squamous cell carcinoma in India is high in male population with male to female sex ratio around 3:1.[80,81,82,83]

A case control study conducted in three areas of southern India (Bangalore, Chennai, Trivandrum) regarding incidence of oral cavity cancer has demonstrated that male to female sex ratio in Bangalore area was the least accounting to 0.5 when compared to other areas of south India. This study has also evaluated the reason for such high incidences in women of this area and attributed it to quid chewing habit of rural women.[80]

The median age group of our study population was 46.5 years and mean age group is 47.5 years.

In a paper published with Ministry of health and family welfare, Government of India, it has been stated that the majority of oral cancer burden is in the age group of 35- 50 years.[81] A

review article comparing various cancer registries of India also showed maximum prevalence of oral cancers in third and fourth decade.[82] A study conducted in South India showed median age of male OSCC subjects was 56 years and median age for female population was 58 years.[80] A similar clinico-pathological study conducted in North India showed a mean of 48.35 years.[84]

66.6% of our study population presented with advanced disease (T4a) and 33.3% of subjects were stage T3 tumors. A study performed in a regional cancer center also showed similar findings where 60% of OSCC patients presented with T4a tumors while 30% presented with T3 tumors.[84]This late presentation to speciality surgical center may be attributed to lack of medical education, negligence and low literacy rates among majority of study population.[81,82]

It has already been proven by many studies that direct exposure of irradiation to nasal mucosa (nasopharyngeal carcinoma, nasal and paranasal sinus carcinoma) where the field of irradiation includes majority of nasal cavity and paranasal sinuses, hampers mucociliary clearance and subsequently leads to development of chronic rhinosinusitis in these patients.[3,4,5,6] A Chinese study showed that the occurrence rates of paranasal sinusitis at first month, third month, sixth month and one year after radiotherapy were 21.0, 33.7, 41.5 and 29.3% respectively.[87]

There is fair evidence suggesting that radiation induced chronic rhinosinusitis leads to long term quality of life impairment.[5]

Our study was designed to evaluate MCC in maxillary antrum which lies adjacent to the field of radiation in post operative patients with squamous cell carcinoma of buccal mucosa. There

is paucity in literature regarding studies which evaluated maxillary antral mucociliary clearance during radiotherapy to adjacent area over the head and neck region.

Studies showed reduction in nasal clearance times in patients receiving radiation where nasal mucosa was in close proximity to field of radiation but not included in it. A Turkish study showed elevated nasal STT in patients who received radiotherapy for laryngeal cancers[70] and an Indian study showed similar results for hypopharyngeal, laryngeal and buccal cancer subjects.[7]

An Italian study which evaluated nasal STT in children who underwent radiation therapy for various head and neck tumours (leukemias, lymphomas, CNS tumors and rhabdomyosarcoma) demonstrated elevated STT post treatment.[71]

Our study shows that adequate assessment of maxillary antral mucociliary clearance can be done by performing two tests namely STT and MTT. Many studies in literature showed that STT and MTT are adequate tools for MCC measurement in nasal mucosa including the landmark study by Messerklinger.[42,46,47,55]

Pre radiotherapy mean STT in ipsilateral and contra lateral antra were 45.17 and 44.79 minutes respectively, while pre radiotherapy MTT in ipsilateral and contra lateral antra were 16.25 and 17.08 minutes.

There is paucity of literature regarding quantification of transit times in maxillary antra. A study done in Finland demonstrated that MTT in maxillary antrum is 13.71 minutes STT is 20 minutes in uncinectomy subjects. The exact procedure of the tests, area of placement of dye and saccharin were not described in this study.[85] A Japanese study demonstrated normal STT to be around 40 minutes and India ink expulsion time of around 30 minutes.[60] The

technique used in measurement of ciliary clearance times in this study is similar to the techniques used in our study and the results measured before radiotherapy in our study were consistent with the Japanese study.

CT scan evidence of mucosal abnormalities following radiation in nasopharyngeal carcinoma patients was also established by some studies. They demonstrated increased Lund Mckay scores following radiation.[65,66,67,68,69]

In our study STT in ipsilateral antra on the side of radiation shows significant elevation beginning from second week of radiotherapy following which throughout the treatment period STT values were above 100 minute mark, suggesting severe diminution in ciliary clearance. Similar trend was shown in MTT values rising from second week of radiation and persistently remained over 50 minutes throughout treatment period. The maximum residual delay in STT during radiation was 63.29 minutes which was recorded during 5^{th} week of treatment. The maximum residual delay in MTT was 40 minutes observed during 6^{th} week of treatment. These findings suggest that maximum deterioration of mucociliary clearance was occurring towards the completion of radiotherapy.

A Japanese study demonstrated that on ultra structural level there is significant loss of ciliary epithelium when STT is above100 minutes.[60] An Egyptian study shows that there is a steep elevation of nasal STT from a mean of 25 minutes to 35 minutes along the course of radiotherapy for nasopharyngeal carcinoma. It also demonstrated that the maximum deterioration in MCC was occurring towards the end of treatment course. [86]

Our results show there is a statistically significant reduction in mucociliary clearance of maxillary antra on the side of radiotherapy suggesting that even though antral epithelium was

not in the field of radiation, the adjacent maxillary antra were affected due to irradiation to tumour area.

Our study shows improvement of residual delay of STT from 61.65 minutes at 6th week to 51 minutes at 3rd month following completion of radiation treatment. Similarly residual delay of MTT improved from 40 minutes to 33.33 minutes at 3rd month post RT. Although MCC indicators did not return back to the baseline (pre radiotherapy values), we have observed a downward trend.

A similar trend in nasal STT was demonstrated from a Turkish study where the mean nasal STT was 16.8 minutes at 3rd month post RT and at 6th month post RT it was found to be 13.4 minutes, suggesting a downward trend of residual delay from 7.7 minutes to 4.3 minutes .[70]

This downward trend was not observed in nasopharyngeal carcinoma patients who received radiation therapy, where it was persistently elevated even after followup for 3 years after completion of radiation[3,4,5]

One study has demonstrated long term effects of radiation on MCC lasting an average duration of 5.9 years following initial treatment. This study also demonstrated the pathologic findings which included epithelial sloughing, ciliary loss, ciliary dysmorphism, vacoulations, collagen fibre deposition in lamina propria, epithelial metaplasia for a significant duration after the completion of radiotherapy.[3]

In our study on the contra lateral side i.e, non irradiated maxillary antra, pre radiotherapy mean STT and mean MTT were 44.79 and 17.08 minutes respectively, Maximum elevation of these recordings were 50.38 and 21.67 respectively towards the end of the radiotherapy treatment course and 3rd month post RT values were 44.08 and 19.17 minutes. Even though

there are slightly reduced clearance times during radiotherapy there is no statistically significant establishment of such findings.

On contrary to our results where MTT and STT on non irradiated side were not considerably affected, few studies have revealed a statistically significant difference between saccharin perception times of pre and post irradiated head and neck cancer patients.[3,4,5] One study suggested that there is development of contralateral sinus mucosal thickening when evaluated using Lund Mckay grading system after completion of radiation to unilateral para nasal sinus malignancy.[8]

Another study compared between clearance times in laryngeal cancer and nasopharyngeal cancer subjects. Mean Nasal STT was elevated from 9.1 minutes pre RT to 16.8 minutes post RT in laryngeal cancer subjects whereas its elevated from 9.7 minutes to 26.1 minutes in nasopharyngeal cancer subjects in bilateral nasal mucosa.

Disparity in results on the non irradiated side may be due to specific consideration of including only buccal mucosa carcinoma patients in our study. PNS and nasopharynx involve some amount of direct radiation to nasal and maxillary mucosa which in turn significantly affects mucociliary clearance in those areas. But, when contralateral antral clearance in patients receiving radiotherapy for squamous cell carcinoma of buccal mucosa is considered, as the contralateral antral mucosa was not included in the field of radiation there were no findings of statistically significant decrease in MCC recorded, there was no statistically significant decreased MCC were recorded because contralateral maxillary antrum wasn't included in the field of radiation.

Results of our study showed that the majority of the study subjects had nausea, mucositis and dry desquamation throughout the period of RT while dysphagia was observed only towards the end of radiation therapy course. Majority of study subjects did not demonstrate any signs of pharyngeal oedema, laryngeal oedema, fungal infection, dysphonia, osteoradionecrosis and hemopoietic suppression. Major fraction of study subjects had neck contractures at 3rd month after completion of RT. Studies show a similar results regarding complications due to radiation to head and neck region.[62,63]

CONCLUSION

CONCLUSION

It is the responsibility of the surgeon to improve the long term quality of life of head and neck cancer patients. Radiation induced sinustitis is a well established complication in patients who have direct radiation exposure to nasal and para nasal sinus mucosa.

Our study establishes that

- Adequate assessment of mucociliary clearance can be done in maxillary antra of patients receiving radiotherapy for buccal mucosa cancers using STT and MTT.
- Mucociliary clearance times in adjacent maxillary antrum to the field of radiation in post operative buccal mucosa carcinoma patients had a statistically significant elevation during radiotherapy.
- MTT and STT were significantly elevated in the ipsilateral antra from 2^{nd} week of radiotherapy.
- Our study shows improvement of residual delay of STT from 61.65 minutes at 6^{th} week to 51 minutes at 3^{rd} month following completion of radiation treatment. Similarly residual delay of MTT improved from 40 minutes to 33.33 minutes. Although MCC indicators did not return back to the baseline (pre radiotherapy values), we have observed a downward trend.
- Contra lateral antra had no significant changes in MTT and STT compared to pre radiotherapy recordings.

When considering surgical drainage procedures for radiation induced sinusitis it is to be kept in mind that the concept of successful FESS is not applicable to radiation induced

rhinosinusitis as its based on healthy and normal Mucociliary clearance. Taking in to account that reversal of radiation induced changes takes much longer or might not revert back at all, dependant drainage procedures should be considered in such symptomatic individuals.

SUMMARY

SUMMARY

This study was done on patients with T_3 ,T_{4a} squamous cell carcinoma of buccal mucosa operated with curative intent and planned to receive postoperative radiotherapy admitted under Department of Otorhinolaryngology and Head and Neck Surgery ward of R L Jalappa Hospital and Research Centre , ,Kolar during period of Dec 2015-Jul 2017.

Patients were selected based on the inclusion and exclusion criteria and bilateral Middle Meatal Antrostomy was performed during the oncosurgical procedure.

Mucociliary clearance time was measured by placing methylene blue and saccharine crystal in maxillary antra (bilateral) and periodic endoscopy was performed to study the mucociliary clearance. [just before starting radiotherapy, weekly during radiotherapy and 1 and 3 months post radiotherapy].

- Mucociliary clearance times through Methylene blue Transit Time and Saccharine Transit Times were statistically compared between pre radiation values and values during radiation and follow up.
- Mucociliary clearance times in ipsilateral maxillary antra (case) were compared with contralateral maxillary antra (control).
- Incidence and duration of other side effects of radiation like nausea, dysphagia, dysphonia, pharyngeal and laryngeal odema, skin reactions, mucositis, osteoradionecrosis and hemopoietic suppression were recorded during MCC measurements.
- Significant positive co relation between radiation exposure and reduction in MCC was observed on the ipsilateral side.

- Statistically insignificant findings observed on the non radiated side.
- Significant increase of clearance times observed from second week of radiation therapy.
- Minimal recovery of MCC observed during the follow up period which was statistically insignificant.

BIBLIOGRAPHY

LIST OF REFERENCES

1.Ramesh C. *Hospital Based Cancer Registry* .Kidwai Memorial Institute of Oncology;2005

2. Kalyani R, Das S, Bindra Singh MS, Kumar H. Cancer profile in Kolar: A ten years study. Indian J Cancer 2010; 47:160-5.

3.Lou PJ,Chen WP, Tai CC .Delayed irradiation effects on nasal epithelium in patients with nasopharyngeal carcinoma . Annal Otorhinolaryngol 1998,108;474-80.

4. Stringer SP, Stiles W, Slattery WH 3rd, Krumerman J, Parsons JT, Mendenhall WM, et al. Nasal mucociliary clearance after radiation therapy. Laryngoscope 1995;105:380-2.

5. Eran Alon E, Lipschitz N, Bedrin L, Gluck I, Talmi Y, Michael Wolf, Yakirevitch A. Delayed Sino-nasal Complications of Radiotherapy for Nasopharyngeal Carcinoma. Otolaryngol Head Neck Surg 2014, Vol. 151(2) 354–358.

6. Stammberger H. Endoscopic endonasal surgery: concepts in treatment of recurring sinusitis. l.Anatomic and pathophysiological considerations. Otolaryngol Head Neck Surg 1986; 94: 143-147.

7.Gupta SC, Chandra S, Singh M. Effects of irradiation on nasal mucociliary clearance in head and neck cancer patients. Indian J Otorhinolaryngol Head Neck Surg.2006;58:46-50.

8. Wang JH, Lee BJ, Lee JH, Kim IJ, Jang YJ. Development of mucosal thickening after radiotherapy in contralateral sinuses of patients with nasal cavity and/or paranasal sinus carcinoma. Annal Otol Rhinol Laryngol 2008;117(11):844-848.

9. Ackerknecht EH. Historical notes on cancer. Med Hist 1958; 2: 114–119.

10. Butterfield WC. Tumor treatment, 3000 B.C.. Surgery 1966;60:4769.

11. Kardinal CG. An outline of the history of cancer. Part I. Mo Med 1977;74:6626.

12. Redmond DE. Tobacco and cancer: the first clinical report, 1761. N Engl J Med 1970; 282: 18–23.

13. Pott P. Chirurgical Works of Percivall Pott, FRS and Surgeon to St Bartholomew's Hospital. London: Lowndes, 1775: 734–736.

14. Sömmerring ST. De morbis vasorum absorbentium corporis humani [etc]. Trajectinae ad Moenum; Varrentrappii et Wenneri, 1795; 109.

15.Roentgen WC. Ueber Eine Neue Art von Strahlen. Sitzungsberichte der Physikalisch-Medicinischen Gesellschaft zu Wurzberg, 1895. Sitzun 1895; 30: 132–141.

16.Buschke F. Radiation therapy: historical perspectives. Radiol Clin Biol 1971; 40: 217–220.

17. Paterson R, Parker HM. A dosage system for gamma ray therapy. Br J Radiol 1934; 7: 592–632.

18. Coutard H. Roentgentherapie des epitheliomas de la region amygdalienne, de l' hypopharynx et du larynx au cours des anees 1920 a 1926. Radiophysiologie et Radiotherapie. Paris, France 1930–32; 2: 541–575.

19. Fletcher GH. History of irradiation in squamous cell carcinomas of the larynx and hypopharynx. Int J Radiat Oncol Biol Phys 1986;12:2019–24.

20. Butlin HT. What operation can do for cancer of the tongue. Br Med J 1898; 541–544.

21. Butlin HT. On the early diagnosis of cancer of the tongue, and on the results of operations in such cases. Br Med J 1909; 462–463.

22. Crile G. Excision of cancer of the head and neck: with special reference to the plan of dissection Based on one hundred and thirty two operations. J Am Med Assoc 1906; 47: 1780–1788.

23. Cade S. Radium Treatment of Cancer. London: J and A Churchill, 1929; 29.

24. Butlin HT, Spencer WG. Diseases of the tongue. 2nd ed. London: Cassell & Company; 1900., p. 392.

25. Martin H, Del Valle B, Ehrlich H, Cahan WG. Neck dissection. Cancer 1951;4:441–99.

26.Ferlito A, Gavila´n J, Buckley JG, Shaha AR, Miodonski AJ, Rinaldo A. Functional neck dissection: fact and fiction. Head Neck 2001;23:804–8.

27. Ferlito A, Rinaldo A. Osvaldo Sua´rez: often-forgotten father of functional neck dissection (in the non-Spanish-speaking literature). Laryngoscope 2004;114:1177–8.

28. Ferlito A, Rinaldo A. Neck dissection: historical and current concepts. Am J Otolaryngol 2005;26:289–95.

29. Ferlito A, Rinaldo A, Robbins KT, Silver CE. Neck dissection: past, present, and future? J Laryngol Otol 2006;120:87–92.

30. Ferlito A, Rinaldo A, Silver CE, Shah JP, Sua´rez C, Medina JE, et al. Neck dissection: then and now. Auris Nasus Larynx 2006;33:365–74.

31. Chim H, Salgado CJ, Seselgyte R, Wei FC, Mardini S. Principles of head and neck reconstruction: an algorithm to guide flap selection. InSeminars in plastic surgery 2010 May (Vol. 24, No. 02, pp. 148-154). © Thieme Medical Publishers.

32. Beech R, Reid J, Fung H, Heffez L. Anteriorly Based Tongue Flap for Closure of a Posterior Palatal Defect in a Patient with Exaggerated Gag Reflex. World Journal of Medical and Surgical Case Reports. 2015 Sep 25;4(10).

33. Güerrissi JO. Lateral deltopectoral flap: a new and extended flap. Journal of Craniofacial Surgery. 2009 May 1;20(3):885-8.

34. Ariyan S. The pectoralis major myocutaneous flap: a versatile flap for head and neck reconstruction. Plast Reconstr Surg 1979; 63:73-81.

35. Ramsey KW, Georgeu GA, Pereira JA, El-Muttardi N. Nasal reconstruction in the Yemen with the Converse scalping flap. Journal of the Royal Society of Medicine. 2003 May 1;96(5):230-2.

36.McGregor IA. The temporal flap in intra-oral cancer: its use in repairing the post-excisional defect. British Journal of Plastic Surgery. 1963 Jan 1;16:318-35.

37. Banzet P, Bricout N, Chretten B, Servant JM. The Chinese forearm flap of continuous vascular pedicle flap.(French). Plastic and Reconstructive Surgery. 1987 Apr 1;79(4):681.

38. Netter FH. Atlas of human anatomy. Elsevier Health Sciences; 2010 May 3.

39. Robbins KT. Classification of neck dissection: current concepts and future considerations. Otolaryngologic Clinics of North America. 1998 Aug 1;31(4):63955.

40. Stammberger H, Lund VJ. Anatomy of nose and paranasal sinuses. In:Gleason M, editor. Scott Brown's Otolaryngology and Head and Neck surgery. 7th ed. Great Britain. Hodder Arnold 2008;1315-1343

41. Stammberger H. Special endoscopic anatomy of the lateral nasal wall and ethmoidal sinuses. Functional Sinus Surgery. BC Decker Philadelphia. 1991:49-87.

42. P. Cole, Physiology of the nose and paranasal sinuses, Clin. Rev. Allergy Immunol. 16 (1998) 25–55

43. N.S. Jones, D. Rog, Olfaction: a review, J. Laryngol. Otol. 112 (1998) 11–24.

44. T.R. Cooney, A.P. Huisson, R.J. Powell, N.S. Jones, Investigations for immunodeficiency in patients with recurrent ENT infections, Clin. Otolaryngol. 26 (2001) 1–5.

45. D.L. Swift, Physical principles of airflow and transportphenomena influencing air modification, in: D.F. Proctor, I. Anderson (Eds.), The Nose: Upper Airway Physiology andthe Atmospheric Environment, Elsevier, Amsterdam, 1982pp. 337347.

46. Stammberger H. Secretion transportation.In Hawke M, editor. Functional endoscopic sinus surgery: The Messerklinger technique. 1st ed. .BC.Decker Philadelphia.1991:17-48

47. Hilding, A.: (a) Ciliary Activity and Course of Secretion of the Nose, Proc. Staff Meet., Mayo Clin. 6:285 (May 13) 1931. (b) The Physiology of Drainage of Nasal Mucus : I. The Flow of the Mucus Currents Through the Drainage System of the Mucosa and Its Relation to Ciliary Activity, Arch. Otolaryng. 15:92 (Jan.) 1932.

48. Hamed R, Fiegel J. 2014. Synthetic tracheal mucus with native rheological and surface tension properties. J Biomed Mater Res A 102: 1788–1798.

49. Matthews LW, Spector S, Lemm J, Potter JL. 1963. Studies on pulmonary secretions. Am Rev Respir Dis 88: 199–204

50. Tarran R, Button B, Picher M, Paradiso AM, Ribeiro CM, Lazarowski ER, Zhang L, Collins PL, Pickles RJ, Fredberg JJ, et al. 2005. Normal and cystic fibrosis airway surface liquid homeostasis: The effects of phasic shear stress and viral infections. J Biol Chem 280: 35751–35759.

51. Brekman A,Walters MS, Tilley AE, Crystal RG. 2014. FOXJ1 prevents cilia growth inhibition by cigarette smoke in human airway epithelium in vitro. Am J Respir Cell Mol Biol 51: 688–700

52. SatirP, ChristensenST. 2007. Overview of structure and function of mammalian cilia. Annu Rev Physiol 69: 377–400.

53. Heuser T, Raytchev M, Krell J, Porter ME, Nicastro D. 2009. The dynein regulatory complex is the nexin link and a major regulatory node in cilia and flagella. J Cell Biol 187: 921–933.

54. Chilvers MA, O'Callaghan C. 2000. Analysis of ciliary beat pattern and beat frequency using digital high speed imaging: Comparison with the photomultiplier and photodiode methods. Thorax 55: 314–317.

55.Adam Wanner "Clinical Aspects of Mucociliary Transport", American Review of Respiratory Disease, Vol. 116, No. 1 (1977), pp. 73125.

56. Paltieli Y, Fradis M, Ben-David J, Podoshin L, Shiti H, Kam Z. In vivo measurement of human nasal mucociliary motility using a laser light scattering instrument. Annal Otol Rhinol Laryngol 1997;106:859-861

57. Hilding A. Ciliary Activity and Course of Secretion Currents in the Nose. Proc Mayo Clin 1931; 6:825.

58.Tremble GE. Clinical Observations in The Movement of Nasal Cilia. An Experimental Study. Laryngoscope 1948;58:206.

59.Andersen I, Lundqvist G, Proctor DF. Human Nasal Function in a Controlled Climate. Archs Envir Hlth 1971;23(6):408-20.

60.Asai K, Haruna S, Otori N, Yanagi K, Fukami M, Moriyama H (2000) Saccharine test of maxillary sinus mucociliary function after endoscopic sinus surgery. Larygoscope 110(1):117–122

61. Proctor DF, Wagner HN Jr. Clearance of Particles from the Human Nose. Archs Envir Hlth 1965;11:366.

62.Cooper JS, Pajak TF, Forastiere AA . Postoperative concurrent radiotherapy and chemotherapy for high-risk squamous-cell carcinoma of the head and neck. NEJM 2004; 350: 1937–44.

63.Bernier J, Domenge C, Ozsahin M . Postoperative irradiation with or without concomitant chemotherapy for locally advanced head and neck cancer. NEJM 2004; 350: 1945–52.

64. Robertson AG .Early closure of a randomized trial: surgery and postoperative radiotherapy versus radiotherapy in the management of intra-oral tumours. Clin Oncol (R Coll Radiol) .1998; 10(3):155–160.

65.Porter MJ, Cheung HS, Ambrose R, et al. Abnormalities of the paranasal sinuses in patients with nasopharyngeal carcinoma: a computed tomographic study. J Laryngol Otol 1996;110:23–26.

66.Porter MJ, Leung SF, Ambrose R, et al. The paranasal sinuses before and after radiotherapy for nasopharyngeal carcinoma: a computed tomographic study. J Laryngol Otol 1996;110:19 –22.

67. Avrahami E, Frishman E, Weiss-Peretz J. CT evidence of mucosal thickening in the maxillary antra in patients with nasopharyngeal carcinoma. AJNR Am J Neuroradiol 1991; 12:275–278.

68. Chang CC, Chen MK, Wen YS, et al. Effects of radiotherapy for nasopharyngeal carcinoma on the paranasal sinuses: study based on computed tomography scanning. J Otolaryngol 2000;29:23–27.

69. Kamel R, Al Badawy S, Khairy A, et al. Nasal and paranasal sinus changes after radiotherapy for nasopharyngeal carcinoma. Acta Otolaryngol 2004;124:532–535.

70. Kılıç, C., Tunçel, Ü., Cömert, E. et al. The effect of radiotherapy on mucociliary clearance in patients with laryngeal and nasopharyngeal cancer. Eur Arch Otorhinolaryngol (2015) 272: 1517.

71. Surico G, Muggeo P, Mappa L, Muggeo V, Conti V, Lucarelli A et al (2001) Impairment of nasal mucociliary clearance after radiotherapy for childhood head cancer. Head Neck 23(6):461–466.

72. Saif M W, Edward C. Pharmacology of cancer therapeutics/chemotherapy agents ;antimetabolites. In: Vincent T, Devita Jr, Theodore S.Lawrence, Steven A.Rosenberg, editors. DeVita, Hellman and Rosenberg's Cancer: Principles and practice of oncology . 9th ed. Philadelphia USA; 2013. p. 393-401.

73. Kennedy DW, Zinreich SJ, Shaalan H, Kuhn F, Naclerio R, Loch E. Endoscopic middle meatal antrostomy: theory, technique, and patency. Laryngoscope. 1987 Aug;97(8 Pt 3 Suppl 43):19.

74. Hall, E. J., "Radiobiology for the radiologist", Lippincott, Philadelphia, Pennsylvania, U.S.A. (2000).

75. Nias, A.W.,"An introduction to radiobiology", Wiley, New York, New York, U.S.A. (1998).

76. Steel, GG., "Basic clinical radiobiology", Arnold, London, United Kingdom (2002).

77. van Dyk J, Battista JJ. Cobalt-60: An old modality, a renewed challenge. Curren Oncology. 1996;3:8–17.

78. Glasgow GP. Cobalt-60 Teletherapy. In: van Dyk J, editor. The Modern Technology of Radiation Oncology. Madison, WI: Medical Physics Publishing; 1999.

79. Joshi CP, Kerr AT, Schreiner LJ, Salomons GJ. Proc. of 22nd International Conference on Medical Physics and Radiation Safety. Vol. 26. Mumbai, India: Journal of Medical Physics; 2001. An estimation of treatmentimes, source activity and other parameters for a 60Co Tomotherapy Unit; pp. 102–04.

80. Balaram P, Sridhar H, Rajkumar T, Vaccarella S, Herrero R, Nandakumar A, et al. Oral cancer in Southern India: The influence of smoking, drinking, paan-chewing and oral hygiene. Int J Cancer 2002;98:440-445

81. Nair MK, Varghese C, Swaminathan A. Cancer: Current scenario intervention strategies and projections for 2015. In: Burden of Disease in India, Background Papers . New Delhi: National Commission for Macroeconomics and Health, Ministry of Health and Family Welfare, Government of India; 2005. pp. 218–225.

82. Bhawna Gupta1, Anura Ariyawardana2,3 and Newell W. Johnson2 "Oral cancer in India continues in epidemic proportions: evidence base and policy initiatives"International Dental Journal 2013; 63: 12–25

83. Patel MM, Pandya AN. Relationship of oral cancer with age, sex, site distribution and habits. Indian J Pathol Microbiol 2004;47(2):195-197

84. Singh MP, Kumar V, Agarwal A, Kumar R, Bhatt MLB, Misra S. Clinico-epidemiological study of oral squamous cell carcinoma: A tertiary care centre study in North India. Journal of Oral Biology and Craniofacial Research. 2016;6(1):31-34.

85. Bizaki AJ, Numminen J, Taulu R, et al. A controlled, randomized clinical study on the impact of treatment on antral mucociliary clearance; uncinectomy versus balloon sinuplasty. Ann Otol Rhinol Laryngol. May 2016; 125(5):408-414.

86. Kamel R, Al-Badawy S, Kandil T, et al. Nasal and paranasal sinus changes after radiotherapy for nasopharyngeal carcinoma [J]. Acta Otolaryngol, 2004,124(4):532-535.

87. Yuan TZ, Guo X, Zheng L et al (2008) Occurrence and influencing factors of paranasal sinusitis in nasopharyngeal carcinoma patients after radiotherapy. Ai Zheng 27:866–869.

ANNEXURES

INFORMED CONSENT FORM

I, Mr/Mrs have been explained in a language I can understand, that I will be included in a study which is EVALUATION OF MUCOCILIARY ACTIVITY IN MAXILLARY ANTRA IN PATIENTS WITH SQUAMOUS CELL CARCINOMA OF BUCCAL MUCOSA UNDERGOING POST OPERATIVE RADIOTHERAPY.

I have been explained that my clinical finding, investigations, periodic endoscopic evaluation details will be assessed and documented for the study purpose.

I have been made to understand that I will not incur any added expenditure other than investigations, materials and cost for the surgery for the treatment of cancer.

I have also been informed the study will involve an additional endoscopic procedure on my maxillary sinuses, this is a small surgical procedure and its risks, complications and outcomes have been explained in a language understandable to us. This procedure will provide a better drainage for my sinuses.

I have also been made to understand that this study will require a periodic endoscopic evaluation [post operatively, weekly during radiotherapy and 1 and 3 months post radiotherapy].

I have been explained that my participation in this study is entirely voluntary and I can withdraw from the study anytime and this will not affect my relation with my doctor or the treatment for my ailment.

I have understood that all my details found during the study are kept confidential and while publishing or sharing of the findings, my details will be masked.

I, in my sound mind give full consent to be added in the part of this study.

Patients signature/ thumb impression:

1st Witness signature : 2nd witness signature :

DATE: TIME: PLACE:

PROFORMA

EVALUATION OF MUCOCILIARY ACTIVITY IN MAXILLARY ANTRA IN PATIENTS WITH SQUAMOUS CELL CARCINOMA BUCCAL MUCOSA UNDERGOING POST OPERATIVE RADIOTHERAPY - PROFORMA

PERSONAL DETAIL

Name : Age : Sex : M F

Address : Date : Occupation :

Telephone : Hospital no:

E-mail ID :

PRESENTING COMPLAINT

CHIEF COMPLAINTS	YES/NO	SINCE
Presence of ulcer/mass in oral cavity		
Presence of burning sensation in oral cavity upon taking spicy food		
Restricted mouth opening		
Excessive salivation		
Difficulty in swallowing		
Pain in cheek		
Loose of tooth		
Others (specify)		

Lesion Site : Buccal mucosa/ Gingivobuccal sulcus/ Retromolar Trigone/lower gingiva

Side : Right/ Left

HISTORY OF PRESENT ILLNESS

Onset : Progression :

Aggravating factors :

Relieving factors :

H/O trauma : Y/ N

H/O difficulty in swallowing : Y/ N

H/O difficulty in breathing : Y/ N

H/O change in voice : Y/ N

H/O weight loss : Y/ N

PAST HISTORY

H/O Diabetes mellitus, Hypertension, Tuberculosis, Bronchial asthma, Drug allergy

H/O previous surgery: Y/ N

Treatment History (if any): Surgery/ Radiotherapy/ Chemotherapy

FAMILY HISTORY

Contributory ☐ Not contributory ☐

PERSONAL HISTORY

Loss of appetite: Y/ N

Disturbed sleep: Y/ N

Bowel and bladder disturbances: Y/ N

Habits –

- Tobacco chewing :

  Type – Betel nut/ Pan masala/ Gutka

  Duration - Frequency –

  Side – Right/ Left/ Both Leaves overnight – Y/ N

  Tobacco – Y/ N Lime – Y/ N

  Stopped since –

  (if stopped)

- Smoking :

  Type – Filtered Cigarette/ Unfiltered Cigarette/ Beedi/ Hookha/ Pipe

  Duration - Packs/Day -

  Reverse smoking :Y/ N Stopped since –

  (if stopped)

- Alcohol :

  Duration - Type -

  Amount/ day - Stopped since –

  (if stopped)

EXAMINATION

GENERAL PHYSICAL EXAMINATION

Built: Poor/ Medium/ Well-built Nutritional status: Poor/ Satisfactory

Temperature: Pulse: BP: RR:

Pallor: Y/ N Icterus: Y/ N Cyanosis Y/ N

Clubbing: Y/ N Lymphadenopathy: Y/ N Oedema: Y/ N

E.N.T EXAMINATION

- **Oral Cavity :**
  Mouth opening: Adequate/ Trismus Grade of Trismus (if any):

  Oro – dental Hygiene: Poor/ Satisfactory Nicotine stains: Y/ N

  Site: Buccal mucosa/ Retromolar Trigone/Gingivo-buccal Sulcus/lower gingiva

  Side: Right/ Left/ Both

  Type of Lesion: Leukoplakia/ Erythroplakia/ Erythroleukoplakia/ Lichen planus/ Oral Submucous Fibrosis/ Verrucous/ Ulceroproliferative/ Ulcerative

  Bimanual palpation of tumour:

  Tumour mobility over mandible: Y/N

  Fixity of tumour over mandible: Y/N

  Dimension:

  Extent – Superior:

  Inferior:

  Medial:

  Lateral:

  Edge:

  Tender: Y/ N

  Skin involvement: Y/ N

  Bleeds on touch: Y/ N

Level/ s involved: Number:

Size:

Mobile/ Fixed Consistency: Hard/ Firm

- **Nose :**

- **Ear :**

SYSTEMIC EXAMINATION

Cardio vascular system :

Respiratory system :

Abdomen :

Central nervous system :

CLINICAL DIAGNOSIS

INVESTIGATIONS

Hb: RBC: TC: Platelets: DC: N: L: M: E: B: Others:

BT: CT: HIV: Y/ N HbsAg: Y/ N RBS:

CT SCAN/USG NECK

BIOPSY REPORT

FNAC

TREATMENT

Surgery done:

- ☐ Wide excision
- ☐ Hemimandibulectomy
- ☐ Marginal mandibulectomy
- ☐ SOND ☐ MRND ☐ RND

Date of surgery:

Intra-operative findings:

Histo-pathological report:

Of the primary tumour:

Histological type: squamous cell carcinoma

Histopathological garde:

- ☐ Well differentiated
- ☐ Moderately differentiated
- ☐ Poorly differentiated

Proximity of tumour:

Tumour bone infiltration:

Pattern of spread of tumour:

Involvement of cortical bone:

Involvement of marrow:

Bone Margins: ☐ Positive ☐ Negative

Surgical margins: ☐ Positive ☐ Negative

Lymph node status:

Total no of lymph node:

No of positive nodes:

Micro-metastasis (<2mm in diameter): ☐ Present ☐ Not identified

Extra-capsular spread: ☐ Present ☐ Not identified

pTNM staging :

RADIOTHERAPY DETAILS:

Dose –

No. of cycles-

No.of weeks-

PERIODIC ENDOSCOPIC EVALUATION:

	IPSILATERAL ANTRUM		CONTRALATERAL ANTRUM	
	Saccharin transit time	Methylene blue transit time	Saccharin transit time	Methylene blue transit time
Post op				
1st week of radiotherapy				
2nd week				
3rd week				
4th week				
5th week				
6th week				
7th week				
1 month post radiotherapy				
2 months post radiotherapy				

IPSILATERAL ANTRUM:

Mean Saccharin transit time-

Mean methylene blue transit time-

CONTRALATERAL ANTRUM:

Mean Saccharine transit time-

Mean Methylene blue transit time-

PATIENT INFORMATION SHEET

EVALUATION OF MUCOCILIARY ACTIVITY IN MAXILLARY ANTRA IN PATIENTS WITH SQUAMOUS CELL CARCINOMA OF BUCCAL MUCOSA UNDERGOING POST OPERATIVE RADIOTHERAPY

AIM:

To study the mucociliary activity in maxillary antra in patients with squamous cell carcinoma of buccal mucosa undergoing post operative radiotherapy.

PURPOSE:

30-35% of malignancies in India involve head and neck region. Oral cancer accounts for 30% - 45 % of these malignancies. There is a high prevalence of buccal mucosa malignancy in Kolar district due to the habit of betel nut and tobacco chewing and the use of quid. Radiotherapy is a key component in the multidisciplinary treatment approach used in all head and neck cancers. It is associated with many complications out of which sinusitis is one of the significant complication. It needs regular assessment as a routine part of followup.The underlying cause of sinusitis in irradiated patients was proven to be decreased mucociliary clearance in the nasal cavity and paranasal sinuses.We plan to study and document mucociliary clearance in patients receiving post operative radiotherapy for squamous cell carcinoma of buccal mucosa who underwent bilateral middle meatal antrostomy . Based on the findings it may help future studies to decide between middle meatal antrostomy or inferior meatal antrostomy in preventing post irradiation rhinosinusitis.

VOLUNTARY PARTICIPATION: All the information regarding this procedure and the risks associated with it will be explained in detail. After providing all the information, you will be invited to be a part of this study. Your participation in this research is entirely voluntary. It is your choice whether to participate or not. If you choose not to participate in this research project, you will still be offered treatment for the disease

INFORMATION REGARDING THE ENDOSCOPIC DRAINAGE PROCEDURE AND PERIODIC FOLLOW UP:

Then bilateral endoscopic middle meatal antrostomy will be performed under general anaesthesia or local anesthesia at the time of composite resection for squamous cell carcinoma. Mucociliary clearance time will be measured in bilateral maxillary antrums by placing methylene blue and saccharine crystal in maxillary antra (bilateral) and periodic endoscopy will be performed to study the mucociliary clearance. [just before receiving radiotherapy, weekly during radiotherapy and 1 and 3 months post radiotherapy]. Mucociliary clearance in ipsilateral maxillary antrum (case) will be studied comparing with contralateral maxillary antrum

CONFIDENTIALITY: All information collected from you will be kept confidential and will not be disclosed to any outsider. Your identity will not be revealed. This study has been reviewed by the Institutional Ethics Committee and you are free to contact the member of the Institutional Ethics Committee. There is no compulsion to agree to this study. The care you will get will not change if you don't wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study

COMPENSATION AND COST: You will have to pay for the basic investigations and surgical procedures which are routinely done. You will not receive any monetary benefits for participating in this research.

WHO TO CONTACT?If you have any questions you may ask them now or even after the commencement of the study. If you wish to ask questions later, you may contact the following doctor:

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ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳೆ

ಕೆನ್ನೆಯ ಲೋಳೆಪೊರೆಯ ಒಳಪಡುವ ಪೋಸ್ಟ್ ಆಪರೇಟಿವ್ ವಿಕಿರಣ ಚಿಕಿತ್ಸೆಯನ್ನು ಸ್ಕ್ವಾಮಸ್ ಸೆಲ್ ಕಾರ್ಸಿನೋಮ ರೋಗಿಗಳಲ್ಲಿ ಎಲುಬಿನ ANTRA ಇನ್ MUCOCILIARY ಚಟುವಟಿಕೆ ಮೌಲ್ಯಮಾಪನ

AIM:

ಪೋಸ್ಟ್ ಆಪರೇಟಿವ್ ವಿಕಿರಣ ಚಿಕಿತ್ಸೆಯನ್ನು ಪಡೆಯುತ್ತಿರುವ ಕೆನ್ನೆಯ ಲೋಳೆಯ ಸ್ಕ್ವಾಮಸ್ ಸೆಲ್ ಕಾರ್ಸಿನೋಮ ರೋಗಿಗಳಲ್ಲಿ ಎಲುಬಿನ antra ರಲ್ಲಿ mucociliary ಚಟುವಟಿಕೆ ಅಧ್ಯಯನ.

ಉದ್ದೇಶ:

ಭಾರತದಲ್ಲಿ ತೀವ್ರತೆಗಳು 30-35% ತಲೆ ಮತ್ತು ಕುತ್ತಿಗೆ ಪ್ರದೇಶ ಒಳಗೊಂಡಿದೆ. ಈ ತೀವ್ರತೆಗಳು 45% - ಬಾಯಿಯ ಕ್ಯಾನ್ಸರ್ 30% ರಷ್ಟಿದೆ. ಕೋಲಾರ ಜಿಲ್ಲೆಯ ಕೆನ್ನೆಯ ಲೋಳೆಪೊರೆಯ ಉಗ್ರತೆಯಿಂದ ನ ಒಂದು ದೊಡ್ಡ ಪ್ರಭುತ್ವವೇ ಕಾರಣ ಅಡಿಕೆ ಮತ್ತು ತಂಬಾಕು ಮತ್ತು ಚಿಟಿಕೆ ಬಳಕೆಯ ಅಭ್ಯಾಸ ಇಲ್ಲ. ರೇಡಿಯೊ ಎಲ್ಲಾ ತಲೆ ಮತ್ತು ಕೊರಳಿನ ಕ್ಯಾನ್ಸರ್ಗಳು ಬಳಸುವ ವಿಭಿನ್ನ ಶಿಸ್ತುಬದ್ಧತೆಯ ಚಿಕಿತ್ಸೆಯಾಗಿ ಒಂದು ಪ್ರಮುಖ ಅಂಶವಾಗಿದೆ. ಇದು ಮೂಗಿನ ಸೈನಸ್ ನ ಉದ್ರೇಕ ಗಮನಾರ್ಹ ಸಮಸ್ಯೆಯೆಂದರೆ ಒಂದಾಗಿದೆ ಅದರಲ್ಲಿ ಅನೇಕ ಜಟಿಲ ಸಮಸ್ಯೆಗಳಿಗೆ ಕಾರಣವಾಗುತ್ತದೆ. ಇದು ಅಧ್ಯಯನ ಮತ್ತು ಸ್ಕ್ವಾಮಸ್ ಫಾರ್ ಪೋಸ್ಟ್ ಆಪರೇಟಿವ್ ವಿಕಿರಣ ಚಿಕಿತ್ಸೆಯನ್ನು ಪಡೆದ ರೋಗಿಗಳಲ್ಲಿ mucociliary ತೆರವು ದಾಖಲಿಸಲು ಮೂಗಿನ ಕುಳಿಗಳಿಗೆ ಮತ್ತು paranasal sinuses.We ಯೋಜನೆಯಲ್ಲಿ mucociliary ತೆರವು ಕಡಿಮೆಯಾಗುತ್ತವೆ ಸಾಬೀತಾಯಿತು ವಿಕಿರಣಕ್ಕೆ ರೋಗಿಗಳಲ್ಲಿ ಸಿನುಸೈಟಿಸ್ ಕಾರಣ ಆಧಾರವಾಗಿರುವ followup.The ದಿನಚರಿಯಾಗಿದ್ದು ರೂಢಿಗತ ಮೌಲ್ಯಮಾಪನ ಅಗತ್ಯವಿದೆ ದ್ವಿಪಕ್ಷೀಯ ಮಧ್ಯಮ meatal antrostomy ಕಂಡಿತು ಕೆನ್ನೆಯ ಲೋಳೆಯ ಸೆಲ್ ಕಾರ್ಸಿನೋಮ. ಸಂಶೋಧನೆಗಳ ಆಧಾರದ ಮೇಲೆ ಇದು ಪೋಸ್ಟ್ ಪ್ರದೀಪನ rhinosinusitis ತಡೆಗಟ್ಟುವಲ್ಲಿ ಮಧ್ಯಮ meatal antrostomy ಅಥವಾ ಕೀಳು meatal antrostomy ನಡುವೆ ನಿರ್ಧರಿಸಲು ಭವಿಷ್ಯದ ಅಧ್ಯಯನಗಳು ನೆರವಾಗಬಹುದು.

ಸ್ವಯಂಪ್ರೇರಿತ ಪಾರ್ಟಿಸಿಪೇಷನ್: ಈ ಕಾರ್ಯವಿಧಾನದ ಬಗ್ಗೆ ಎಲ್ಲಾ ಮಾಹಿತಿ ಮತ್ತು ಅದಕ್ಕೆ ಸಂಬಂಧಿಸಿದ ಅಪಾಯಗಳನ್ನು ವಿವರ ವಿವರಿಸಲಾಗುವುದು. ಎಲ್ಲಾ ಮಾಹಿತಿ ನೀಡುವ ನಂತರ, ನೀವು ಈ ಅಧ್ಯಯನದ ಒಂದು ಭಾಗವಾಗಿದೆ ಎಂದು ಆಮಂತ್ರಿಸಲಾಗಿದೆ. ಈ ಸಂಶೋಧನೆ ನಿಮ್ಮ ಭಾಗವಹಿಸುವಿಕೆ ಸಂಪೂರ್ಣವಾಗಿ ವೈಯಕ್ತಿಕವಾಗಿದ್ದು. ಇದು ಭಾಗವಹಿಸಲು ಇಲ್ಲವೋ ಎಂಬುದನ್ನು ನಿಮ್ಮ ಆಯ್ಕೆಯಾಗಿದೆ. ಈ ಸಂಶೋಧನಾ ಯೋಜನೆಯಲ್ಲಿ ಭಾಗವಹಿಸಲು ಆರಿಸದೇ ಇದ್ದರೆ, ನೀವು ಇನ್ನೂ ರೋಗ ನೀಡಲಾಗುವ

ಎಂಡೊಸ್ಕೋಪಿಕ್ ಒಳಚರಂಡಿ ವಿಧಾನ ಮತ್ತು ಆವರ್ತಕ ಅನುಸರಣೆ ಬಗ್ಗೆ ಮಾಹಿತಿ:

ನಂತರ ದ್ವಿಪಕ್ಷೀಯ ಎಂಡೊಸ್ಕೋಪಿಕ್ ಮಧ್ಯಮ meatal antrostomy ಸ್ಕ್ವಾಮಸ್ ಸೆಲ್ ಕಾರ್ಸಿನೋಮ ಸಮ್ಮಿಶ್ರ ಕತ್ತರಿಸಿದ ಸಮಯದಲ್ಲಿ ಸಾಮಾನ್ಯ ಅರಿವಳಿಕೆ ಅಥವಾ ಸ್ಥಳೀಯ ಅರಿವಳಿಕೆ ಕೈಗೊಳ್ಳಲಾಗುವುದು. Mucociliary ತೆರವು ಸಮಯ ಎಲುಬಿನ antra (ದ್ವಿಪಕ್ಷೀಯ) ಮತ್ತು ಆವರ್ತಕ ಎಂಡೊಸ್ಕೋಪಿ ರಲ್ಲಿ ಮೆತಿಲೀನ್ ಬ್ಲೂ ಮತ್ತು ಭಾವಾತಿರೇಕ ಸ್ಫಟಿಕ ಇರಿಸುವ ಮೂಲಕ ದ್ವಿಪಕ್ಷೀಯ ಎಲುಬಿನ antrums ರಲ್ಲಿ ಅಳೆಯಲಾಗುವುದು mucociliary ತೆರವು ಅಧ್ಯಯನ ಕೈಗೊಳ್ಳಲಾಗುವುದು. [ಕೇವಲ ರೇಡಿಯೊ ಥೆರಪಿ ಮತ್ತು 1 ಮತ್ತು 3 ತಿಂಗಳಲ್ಲಿ ವಿಕಿರಣ ಚಿಕಿತ್ಸೆಯನ್ನು ಸಾಪ್ತಾಹಿಕ ಪಡೆಯುವ ಮುನ್ನ ವಿಕಿರಣ ಚಿಕಿತ್ಸೆಯನ್ನು ಪೋಸ್ಟ್]. ಒಕ್ಕಡೆಯ ಎಲುಬಿನ ಕುಹರದೊಳಗಿನ (ಸಂದರ್ಭದಲ್ಲಿ) ನಲ್ಲಿ Mucociliary ತೆರವು ವಿರುದ್ಧ-ಎಲುಬಿನ ಕುಹರದೊಳಗಿನ ಜೊತೆ ಹೋಲಿಸಿ ಅಧ್ಯಯನ ಮಾಡಲಾಗುತ್ತದೆ

ವಿಶ್ವಾಸಾರ್ಹತೆ: ನೀವು ಸಂಗ್ರಹಿಸಿದ ಎಲ್ಲಾ ಮಾಹಿತಿಯನ್ನು ಗೌಪ್ಯವಾಗಿ ಇಡಲಾಗುತ್ತದೆ ಮತ್ತು ಯಾವುದೇ ಹೊರಗಿನವರ ಬಹಿರಂಗ ಮಾಡಲಾಗುವುದಿಲ್ಲ. ನಿಮ್ಮ ಗುರುತನ್ನು ತೋರಿಸಲಾಗುವುದಿಲ್ಲ. ಈ ಅಧ್ಯಯನವು ನೈತಿಕ ಸಮಿತಿಯ ವಿಮರ್ಶೆ ಮತ್ತು ನೀವು ನೈತಿಕ ಸಮಿತಿಯ ಸದಸ್ಯ ಸಂಪರ್ಕಿಸಲು ಉಚಿತ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಒಪ್ಪಿಕೊಳ್ಳಲು ಯಾವುದೇ ಕಡ್ಡಾಯ ಇಲ್ಲ. ನೀವು ಭಾಗವಹಿಸಲು ಇಚ್ಛಿಸದಿದ್ದರೆ ನೀವು ಪಡೆಯುತ್ತಾನೆ ರಕ್ಷಣೆ ಬದಲಾಗುವುದಿಲ್ಲ. ನೀವು ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಒಪ್ಪುತ್ತೀರಿ ಮಾತ್ರ / ಸೈನ್ ಹೆಬ್ಬೆಟ್ಟಿನ ಗುರುತು ಒದಗಿಸುವುದು ಅಗತ್ಯವಾಗಿದೆ

ಪರಿಹಾರ ಮತ್ತು ವೆಚ್ಚ: ನೀವು ನಿಯಮಿತವಾಗಿ ಮಾಡಲಾಗುತ್ತದೆ ಇದು ಮೂಲ ತನಿಖೆಗಳು ಮತ್ತು ಶಸ್ತ್ರಚಿಕಿತ್ಸಾ ವಿಧಾನಗಳು ಪಾವತಿಸಲು ಹೊಂದಿರುತ್ತದೆ. ಈ ಸಂಶೋಧನೆಯಲ್ಲಿ ಭಾಗವಹಿಸುವ ಯಾವುದೇ ಪರಿಶೀಲನಾ ಲಾಭವನ್ನು ಸ್ವೀಕರಿಸುವುದಿಲ್ಲ.

ನೀವು ಯಾವುದೇ ಪ್ರಶ್ನೆಗಳನ್ನು ಹೊಂದಿದ್ದರೆ, ನೀವು ಅಧ್ಯಯನದಲ್ಲಿ ಶುರುವಾದ ನಂತರ ಈಗ ಅಥವಾ ಅವುಗಳನ್ನು ಕೇಳಬಹುದು? ಯಾರು ಸಂಪರ್ಕಿಸಲು. ನೀವು ನಂತರ ಪ್ರಶ್ನೆಗಳನ್ನು ಕೇಳಲು ಬಯಸಿದರೆ, ನೀವು ಕೆಳಗಿನ ವೈದ್ಯರು ಸಂಪರ್ಕಿಸಬಹುದು:

Dr.Abhimanyu Kadapathri

ಸ್ನಾತಕೋತ್ತರ

ನಾಸಾಕರ್ಣಕಂಠಶಾಸ್ತ್ರ & ತಲೆ ಮತ್ತು ಕುತ್ತಿಗೆ ಶಸ್ತ್ರಚಿಕಿತ್ಸೆ ವಿಭಾಗ

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s.no		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
name		rathnappa	ramappa	ramalakshmamma	krishnamma	jaffer sab	akkamma	gowramma	chikkamallappa	venkateshappa	yellamma	rathnamma	venkatamma	narayanaswamy	noor jan	thimakka	khamrunnisa	mangamma	chandrappa	padmamma	venkatrathnamma	amaravathamma	eeshwaramma	rathnamma	chowdamma
age		45 yr	60 yr	40	36	70 yr	65 yr	36 yr	70 yr	49 yr	50 yr	34	38	50 yr	45	38	42	39	60 yr	48	51	45 yr	52	35	38
sex		male	male	female	female	male	female	female	male	male	female	female	female	male	female	female	female	female	male	female	female	female	female	female	female
hosp.no		280002	256793	356489	396836	275951	342444	376916	252627	366611	364544	389363	265374	392479	245352	123312	354543	235994	281858	347485	326443	388691	418405	274748	257338
	pre radiotherapy	42	40	35	35	40	25	60	40	60	34	45	53	55	48	69	75	35	40	42	20	40	48	63	40
	week 1	60	60	89	40	50	40	70	40	70	47	60	97	90	60	110	90	45	45	45	60	40	46	80	100
	week2	106	80	100	89	120	80	120	90	120	53	120	99	95	95	100	100	55	55	55	89	90	75	120	110
	week 3	96	120	95	82	120	85	102	120	120	83	120	106	105	90	120	110	62	60	87	83	120	110	110	120
ipsi STT	week 4	120	100	78	90	120	120	90	120	120	85	120	109	100	100	120	120	90	90	88	95	120	120	120	110
	week 5	100	110	75	110	120	110	96	120	110	76	120	110	110	100	120	120	107	100	109	110	120	120	120	110
	week 6	90	120	70	110	120	110	87	120	120	69	120	110	110	90	120	120	99	110	105	100	120	120	120	100
	1 month post RT	75	100	62	90	120	90	40	120	120	70	110	120	120	105	100	110	100	100	100	110	120	120	120	100
	3 month post RT	65	100	65	70	120	90	48	120	120	50	110	100	100	95	85	100	100	100	100	120	120	110	120	100
	pre radiotherapy	20	10	10	10	20	10	10	10	30	10	30	20	20	20	20	10	10	20	20	10	10	20	20	20
	week 1	20	10	30	20	40	20	60	30	50	20	30	60	50	40	30	40	10	10	20	40	30	30	50	30
	week2	60	30	50	20	60	40	60	60	50	20	60	60	60	60	60	50	40	60	20	60	60	60	60	50
	week 3	60	40	50	50	60	30	60	60	60	40	60	60	50	60	60	50	50	50	30	60	60	60	60	40
ipsi MTT	week 4	50	40	40	50	60	50	60	60	60	40	60	60	60	50	60	40	50	50	40	60	60	60	60	50
	week 5	60	40	50	50	50	50	60	60	60	40	60	60	60	50	60	40	60	60	30	60	60	60	60	60
	week 6	60	50	40	50	60	50	60	60	60	50	60	60	50	60	60	50	60	60	60	60	60	50	60	60
	1 month post RT	60	40	50	30	60	40	50	60	60	40	50	60	60	60	40	40	60	50	30	60	60	60	60	60
	3 month post RT	40	40	30	30	60	50	40	60	50	40	60	50	50	50	40	50	60	60	30	60	60	60	60	60
	pre radiotherapy	40	30	45	30	30	30	44	30	75	35	60	47	40	62	88	70	25	35	40	30	30	55	59	45
	week 1	45	30	60	30	40	30	50	30	60	45	60	45	55	60	60	60	28	28	30	30	30	58	75	69
	week2	60	20	90	35	60	35	75	40	70	35	80	42	40	54	55	70	24	24	35	40	40	53	70	55
	week 3	57	20	50	55	40	55	71	30	65	39	75	42	40	50	68	70	22	22	67	45	30	60	65	50
contra STT	week 4	72	30	41	40	50	40	50	30	85	29	82	41	40	45	70	60	29	29	48	47	30	55	60	45
	week 5	65	45	55	45	50	45	72	40	65	35	81	30	35	46	65	60	35	35	32	43	40	65	75	50
	week 6	48	35	45	45	55	45	66	30	60	40	76	39	40	55	70	60	30	30	29	45	30	60	70	45
	1 month post RT	42	20	49	60	40	60	48	50	60	40	70	45	45	62	55	50	30	30	30	40	50	45	60	55
	3 month post RT	55	20	40	55	45	55	56	30	65	30	60	50	50	48	49	40	30	30	30	40	30	50	60	40
	pre radiotherapy	20	10	20	10	10	10	20	20	20	10	20	20	20	30	20	20	10	10	20	20	20	20	20	10
	week 1	20	10	30	10	20	10	50	30	20	10	30	10	10	20	30	20	10	10	20	20	30	20	20	20
	week2	30	20	40	10	20	10	40	20	20	10	20	20	20	30	20	20	10	20	10	30	20	30	20	10
	week 3	30	20	40	10	20	10	30	20	20	20	30	20	20	30	30	30	10	10	20	30	20	20	20	10
contra MTT	week 4	20	10	30	10	20	10	30	10	20	30	30	20	20	30	20	30	10	10	20	30	10	20	20	10
	week 5	20	20	30	10	20	10	30	20	20	20	30	20	20	30	20	30	10	20	20	30	20	20	20	20
	week 6	20	20	20	10	20	10	30	30	20	20	30	20	20	20	20	30	10	10	20	30	30	20	20	10
	1 month post RT	20	20	10	20	20	20	30	20	20	30	20	20	20	20	20	30	10	10	10	30	20	20	20	20
	3 month post RT	20	10	20	10	20	10	30	20	20	20	20	30	30	20	20	30	10	10	10	30	20	20	20	10
nausea		nil	nil	week3-6	week 4-6	week 2-6	week 2-6	nil	week 3-6	nil	week 5-6	week 4-6	week 3-6	week 2-6	nil	week 3-6	week 4-6	nil	week 5-6	week 3-6	nil	week 2-6	week 3-6	week 2-6	week 5-6
dysphagia		nil	week 5-6	week 4-6	week 4-6	week 6	week 4-6	week 5-6	week 5-6	nil	week 2-6	week 5-6	week 6	week 4-6	nil	week 6	week 6	week 3-6	nil	week 6	week 3-6	week 6	week 2-6	week 5-6	week 3-6
mucositis		nil	nil	week 3-6	week 4-6	week 6	week 3-6	week 3-6	week 5-6	nil	week 2-6	week 4-6	week 5-6	week 4-6	nil	week 5-6	week 4-6	week 3-6	week 5-6	week 6	week 3-6		week 2-6	week 6	week 2-6
skin reaction		nil	week 5-6	week 4-6	week 4-6	nil	week 2-6	week 3-6	week 3-6	nil	week 5-6	week 2-6	week 3-6	week 4-6	nil	week 2-6	week 4-6	week 2-6	nil	week 4-6	week 2-6	week 2-6	week 5-6	week 4-6	week 2-6
pharyngeal oedema		nil	nil	week 6	week 4-6	nil	week 3-6	nil	nil	nil	nil	nil	nil	nil	nil	week 6	nil	nil	week 6	nil	nil	nil	week 5-6	week 6	week 6
fungal infection		nil	nil	nil	nil	nil	week 6	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil
laryngeal oedema		nil	nil	week 6	week 4-6	nil	week 5-6	nil	nil	nil	week 5-6	week 6	nil	week 6	nil	nil	nil	nil	week 5-6	nil	nil	nil	week 6	nil	nil
dysphonia		nil	nil	week 6	week 4-6	nil	week 6	nil	nil	nil	week 5-6	week 6	nil	week 6	nil	nil	nil	nil	week 6	nil	nil	nil	week 5-6	nil	nil
hematopoietic suppression		nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil
contractures		nil	3rd post op month	3rd post op month	3rd post op month	nil	3rd post op month	3rd post op month	3rd post op month	3rd post op month	3rd post op month	3rd post op month	3rd post op month	3rd post op month	3rd post op month	3rd post op month	3rd post op month	3rd post op month	3rd post op month	3rd post op month	3rd post op month	3rd post op month	3rd post op month	3rd post op month	3rd post op month
osteoradionecrosis		nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil	nil