RADIOTHERAPY IN TOBACCO RELATED LESIONS

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NAMSCON 2016

What is Tobacco ?

- Tobacco is a product prepared by curing tobacco leaves
- Plant belongs to genus *Nicotiana* of the *Solanaceae* family(nightshade)
- > 70 species of tobacco plants are known
- The chief commercial crop is *N. tabacum &* the more potent variant is *N.Rustica*
- *2 types Smoked and Smokeless variety*

Smoked Forms

Smoked forms are consumed through inhalation of smoke

- **Cigarettes** made from cured and finely cut tobacco leaves and reconstituted tobacco, often combined with other additives, then rolled into a paper cylinder
- **Cigars** are tightly rolled bundles of dried and fermented tobacco
- **Beedi** are thin, often flavoured cigarettes (from India) made of tobacco wrapped in a **tendu** leaf

Smoked Forms

- **Hookah** single- or multi-stemmed water pipe for smoking (often glass-based) . A hookah operates by water filtration and indirect heat

- **Pipe** typically consists of a small chamber (bowl) for the combustion of the tobacco to be smoked and a thin stem (shank) that ends in a mouthpiece (bit)

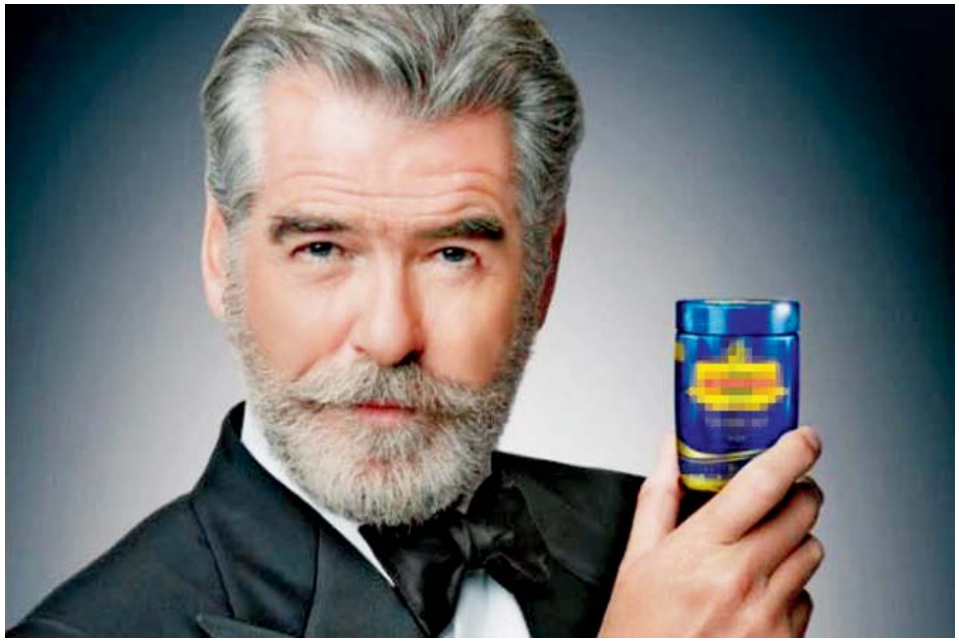
Smoked Forms

KRETEKS

- Cigarettes made with a blend of tobacco, cloves and other flavors
- Originally from Indonesia now used world wide

What is Smokeless Tobacco?

- Smokeless tobacco is tobacco that is not burned
- Also known as chewing tobacco, oral tobacco, spit or spitting tobacco, dip, chew and snuff
- Most people chew or suck (dip) the tobacco in their mouth and spit out the tobacco juices that build up



Smokeless Tobacco

Loose Chewing Tobacco

Plug Chewing Tobacco

- **Chewing tobacco** : consumed orally, 2 forms: sweetened strands, or shredded form
- **Creamy snuffs** : are paste, consisting of tobacco, clove oil, glycerin, spearmint, menthol and camphor. Marketed (to women) in India, brand names Ipco, Denobac, Tona, and Ganesh. Known as *mishri* in some parts of Maharashtra,Goa
- **Dipping tobacco** : A small clump of dip is 'pinched' out of the tin and placed between the lower or upper lip and gums

Smokeless Tobacco

- **Gutka** crushed betel nut, tobacco and sweet or savory flavorings
- **Snuff** is a ground smokeless tobacco product, inhaled or "snuffed" through the nose
- **Snus** is a steam-cured *moist powdered tobacco* that is not fermented, and induces minimal salivation

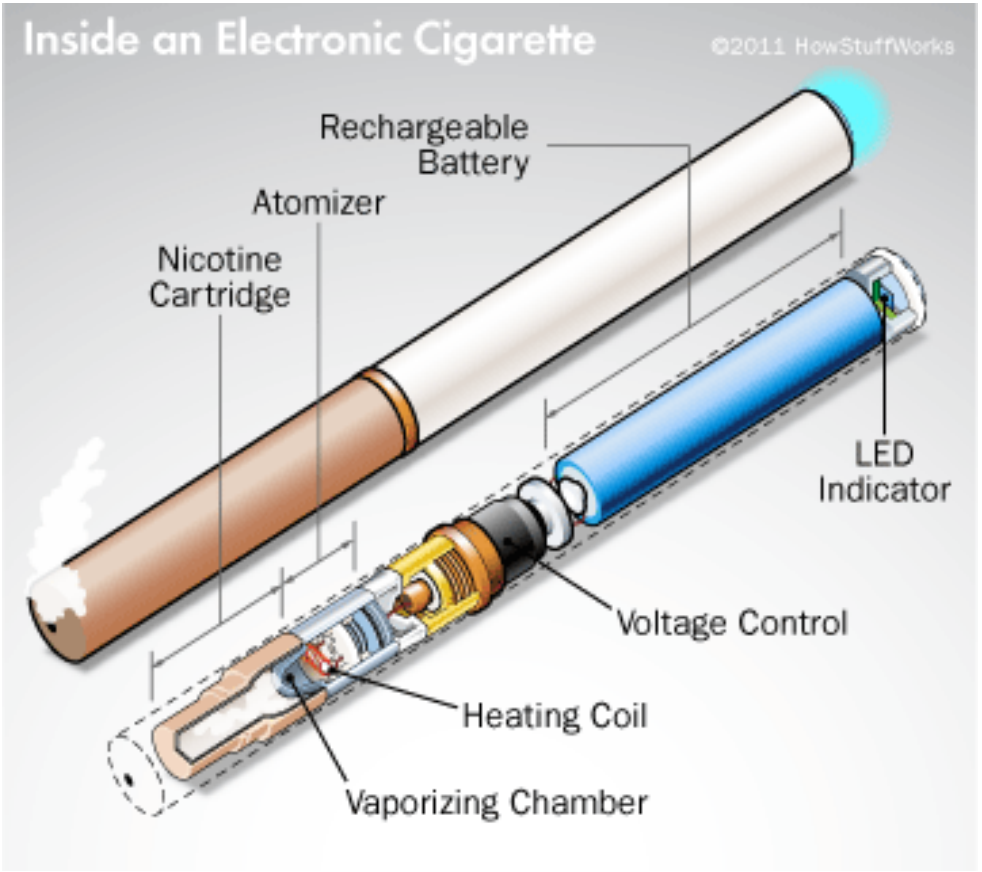
  Consumed by placing it (loose or in little pouches) against the upper gums

Similar to dipping tobacco but does not require spitting and is significantly lower in TSNAs

E-Cigarettes

Electronic Nicotine Delivery System(ENDS)
also called personal vaporizers, vape pens, e-cigars, e-hookah, or vaping devices,

Produce an aerosolized mixture containing flavored liquids and nicotine that is inhaled by the user



Types of tobacco used in India

Smoked forms

Bidis, Cigarettes, Cigars, Cheroots, Chuttas, Dhumti, Hooklis, Chillum & Hookah

Smokeless forms

Paan (betel quid) with tobacco

Paan masala with tobacco

Tobacco, areca nut and slaked lime preparations, Mainpuri tobacco, Mawa, Khaini, chewing tobacco, snus, Gutkha

Tobacco products for application: Mishri, Gul, Bajjar, Lal dantmanjan, Gudakhu, Creamy snuff, Tobacco water, Nicotine chewing gum

Indian Trends

- Beedi smoking is the most popular form of tobacco smoking
- Cigarette smoking is the second most popular
- Paan with tobacco is the major chewing form of tobacco
- Dry tobacco areca nut preparations such as paan masala, gutka and mawa are also popular
- Tobacco dentifrice (lal dant manjan) is popular, especially in some areas and children also use it

Second-hand Smoke & Effects

"Second-hand smoke is smoke from burning tobacco products & smoke that has been breathed out by smokers"

- Causes serious cardiovascular and respiratory diseases and lung cancer
- Causes > 600 000 premature deaths per year (WHO)
- In 2004, children accounted for 28% of the deaths attributable to second-hand smoke
- Second-hand smoke results in 1 in 10 tobacco-related deaths (WHO)

Second-hand Smoke & Cancer

U.S. Environmental Protection Agency

U.S. National Toxicology Program

U.S. Surgeon General

IARC

"SECONDHAND SMOKE AS A KNOWN HUMAN CARCINOGEN"

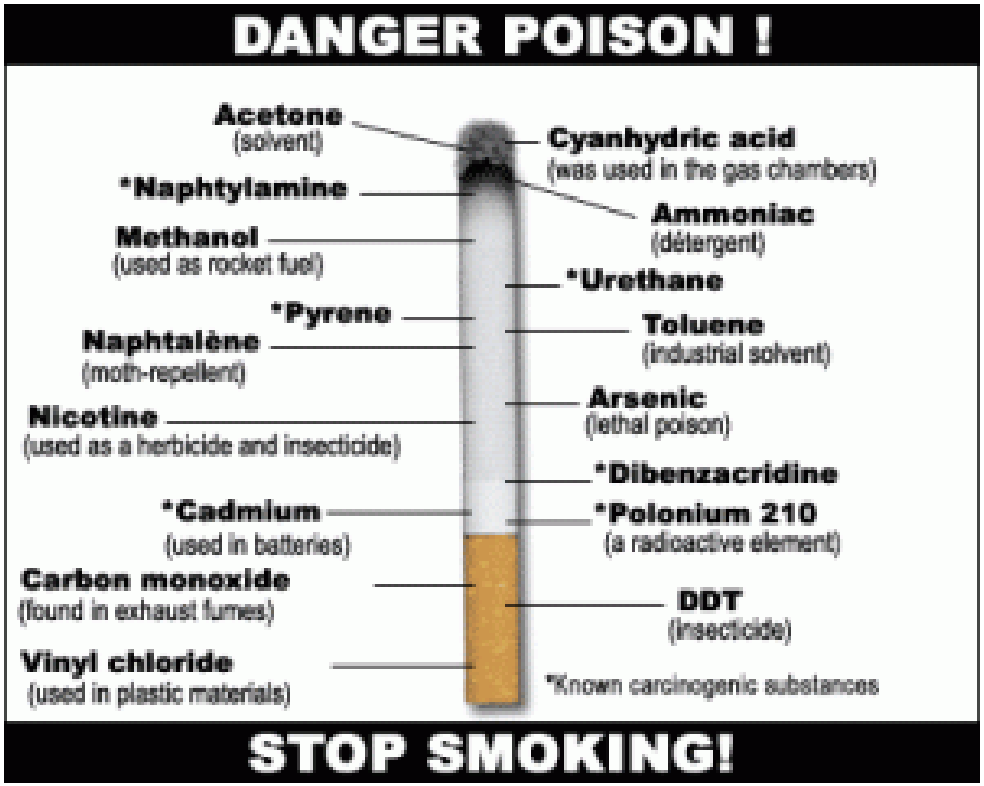
- 3400 lung cancer deaths occur every year among adult nonsmokers in US
- U.S. Surgeon General estimates that living with a smoker increases a nonsmoker's chances of developing lung cancer by 20 to 30%

Tobacco & Cancer

- Tobacco use is leading cause of preventable premature mortality
- It has a particularly profound impact on cancer incidence and mortality
- Tobacco use is causally associated with many different cancers, including lung, head and neck, stomach, pancreas, cervical cancers & others
- Tobacco accounts for 30% of all cancer deaths

Tobacco & Cancer

- There are more than 7,000 chemicals in tobacco smoke
- At least 60 of these chemicals cause cancer
- Most dangerous components
  - Nicotine
  - Tar
  - Carbon monoxide
  - Benzene



Are there harmful chemicals in smokeless tobacco?

- Yes
- There is no safe form of tobacco
- The most harmful chemicals are *tobacco-specific nitrosamines (TSNAs)*, which are formed during the growing, curing, fermenting & aging of tobacco
- Scientists have found that the nitrosamine level is directly related to the risk of cancer
- Polonium–210 (a radioactive element found in tobacco fertilizer) and polynuclear aromatic hydrocarbons (PAH) also carcinogens

Smokeless vs Smoked Tobacco & Cancer

- People who use smokeless tobacco absorb 3-4 times as much nicotine as smokers
- Nicotine is also absorbed more slowly and stays in the blood for a longer time
- *They cause all the hazards of smoking tobacco*
- Smokeless tobacco is more prone to cause oral cavity and pharynx cancer

Major Tobacco Producers

Top tobacco producers, 2012[25]	
Country	**Production (tonnes)**
China	3,200,000
India	875,000
Brazil	810,550
United States	345,837
Indonesia	226,700
Malawi	151,150
Argentina	148,000
Tanzania	120,000
Zimbabwe	115,000
World	**7,490,661.35**

No note = official figure, F = FAO Estimate, A = Aggregate (may include official, semiofficial

WHO Factsheet 2016

Global tobacco use has now assumed pandemic proportions, with about 1.3 billion tobacco users

Key facts

- Tobacco kills around 6 million people each year (50% users)
- More than 5 million of those deaths are the result of direct tobacco use while more than 600 000 killed are non-smokers being exposed to second-hand smoke
- Nearly 80% of the world's 1 billion smokers live in low- and middle-income countries

The GATS Atlas

Global Adult Tobacco Survey

World Health Organization
CDC FOUNDATION
WORLD LUNG FOUNDATION
CDC

Tobacco Use: Prevalence

Among adults age 15 and above *2008–13*

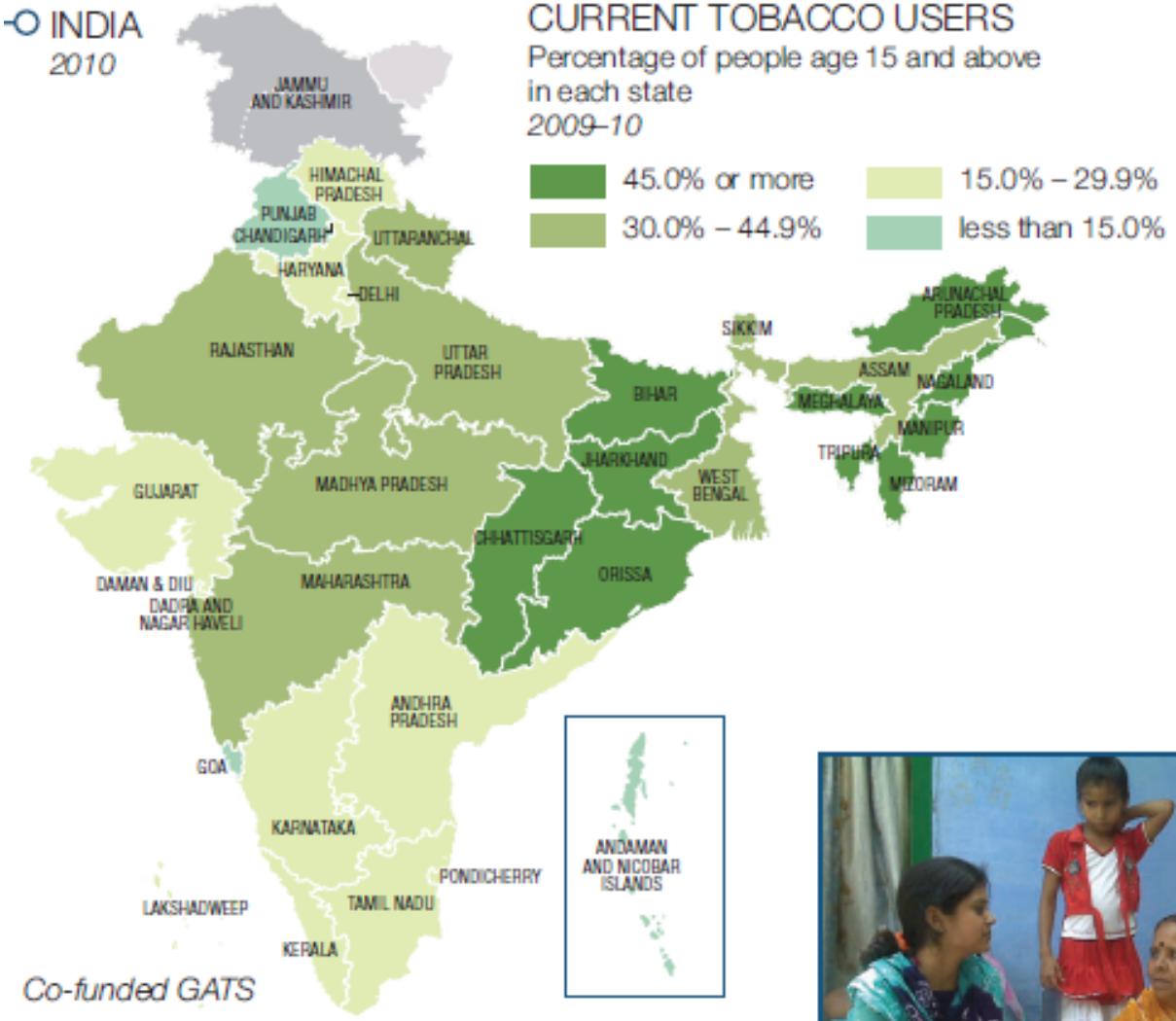
35.0% or more
25.0% – 34.9%
15.0% – 24.9%
less than 15.0%

Source GATS 2015

GATS-India

- As per GAT Survey 48% of males and 20% females use tobacco (any form) in India
- 24% males and 3% females smoke in India
- The overwhelming use of smokeless tobacco globally is in India and Bangladesh
- Worldwide there are 248 million smokeless tobacco users, of which 232 million are from India and Bangladesh
- 206 million in India

Indian Scenario



Co-funded GATS

Highest number of **smokeless tobacco** users (**206 million**) among 22 GATS countries

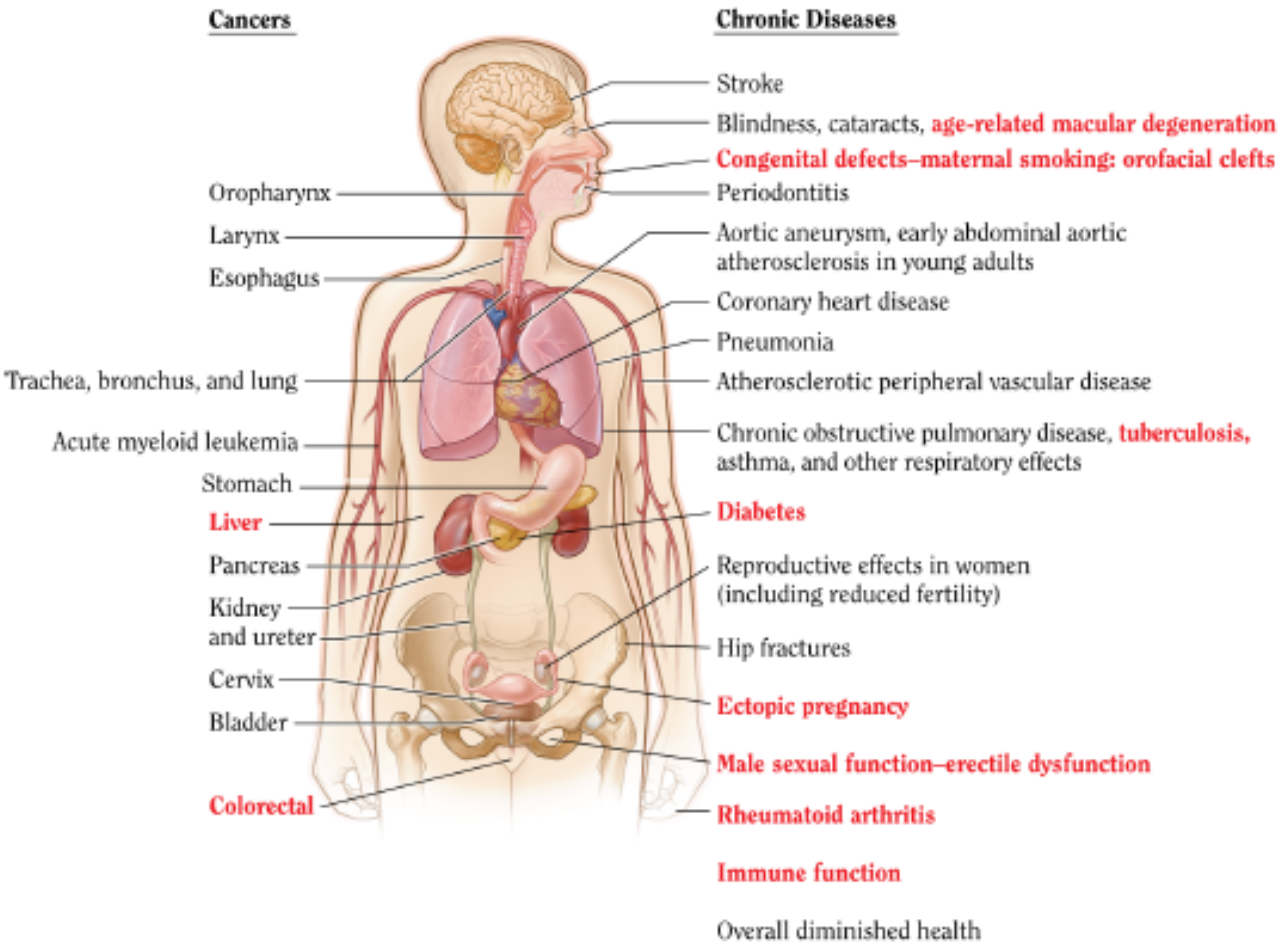
Enforcement of the national **comprehensive tobacco control law** needs further **strengthening**

National, regional, and state-specific estimates are available

▲ *Survey interview in progress in India.*

Report of the Surgeon General 2014

Figure 1A The health consequences causally linked to smoking



Source: USDHHS 2004, 2006, 2012.
Note: The condition in red is a new disease that has been causally linked to smoking in this report.

Report of the Surgeon General 2014

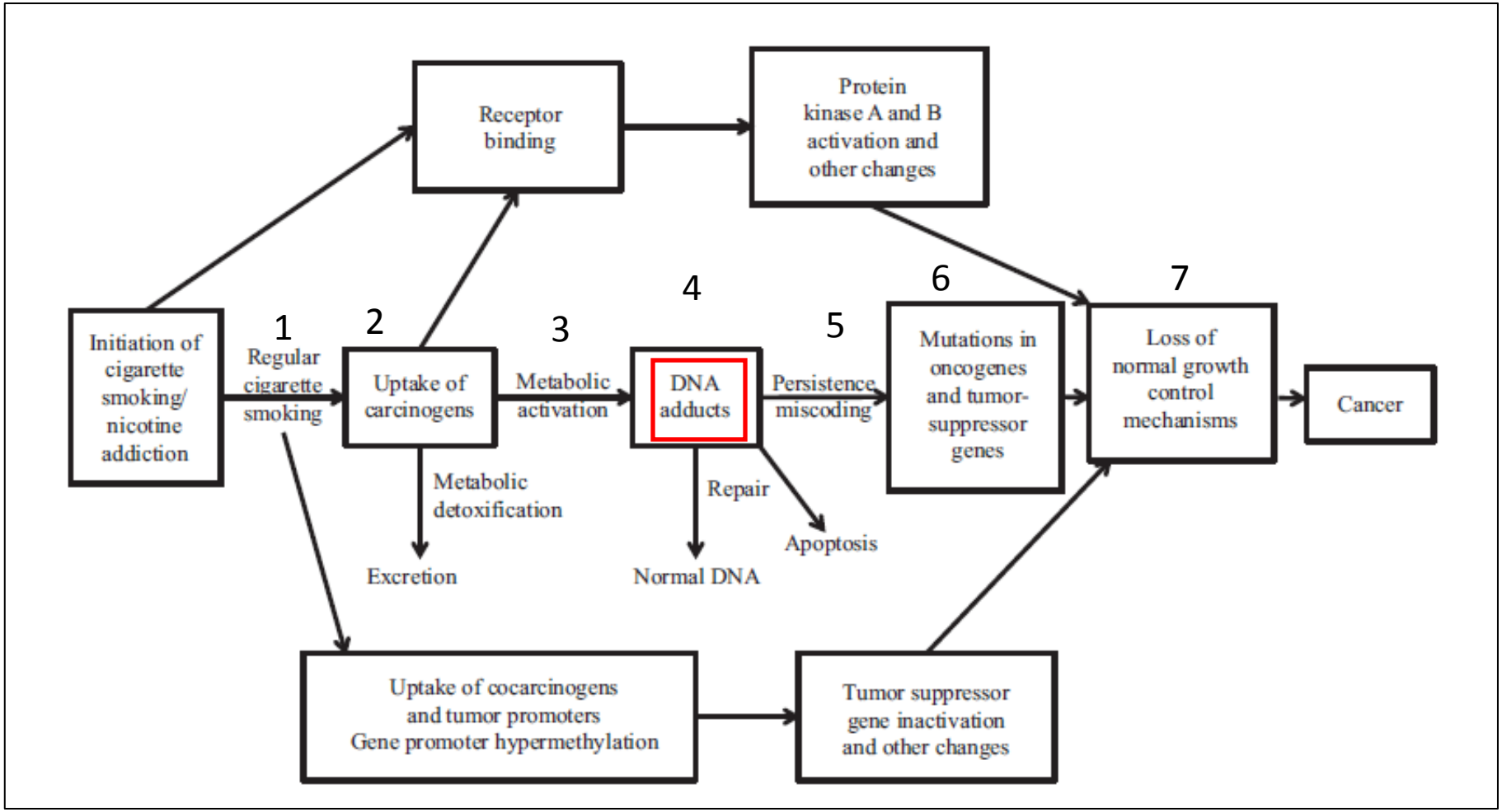
- Evidence is suggestive but insufficient to conclude that smoking and exposure to secondhand smoke causes *breast cancer*
- Smoking is *not a cause for prostate cancer*
- Smoking increases the risk of dying from cancer and other diseases in cancer patients and survivors, including breast and prostate cancer patients

Nicotine Effects

- The major chemical component responsible for addiction to tobacco
- Inhaling smoke induces tissue injury and changes the cellular environment that foster proliferation and transformation cells into cancer cells
- Nicotine triggers cell survival pathways that prevent the death of mutated cells
- It can increase cancer cell proliferation, angiogenesis, migration and invasion

Pechacek and Graham Warren 2012

How Smoking Causes Cancer ?



Role of Radiotherapy In Malignant Lesions/ Cancers

Radiotherapy use can broadly divided as

-External beam radiation therapy(EBRT)

-Brachytherapy

RT- GENERAL PRINCIPLES

- Ionizing radiation produces its biologic effects by direct or indirect effect
- Free radicals are generated, which cause single strand and double strand DNA breaks and loss of cellular reproductive ability & death
- Apoptosis, Mitotic Cell Death
- Most cells do not manifest evidence of damage until mitosis occurs, and several divisions may ensue before actual cell death (termed mitotic cell death)
- For this reason, most tumors do not show immediate shrinkage after starting radiation therapy (RT)
- Radio responsive tumors start to shrink in a few days
- Most head and neck cancers may take weeks or longer to shrink

Role of RT in Head &Neck Cancers

In India about 8 lakh new cases/year Out of them 5.5 lakh H&N cancer

Early Stage

Definitive treatment : Organ preservation

Locally Advanced

Surgery+Postop RT (+/- chemotherapy)

-T3, T4

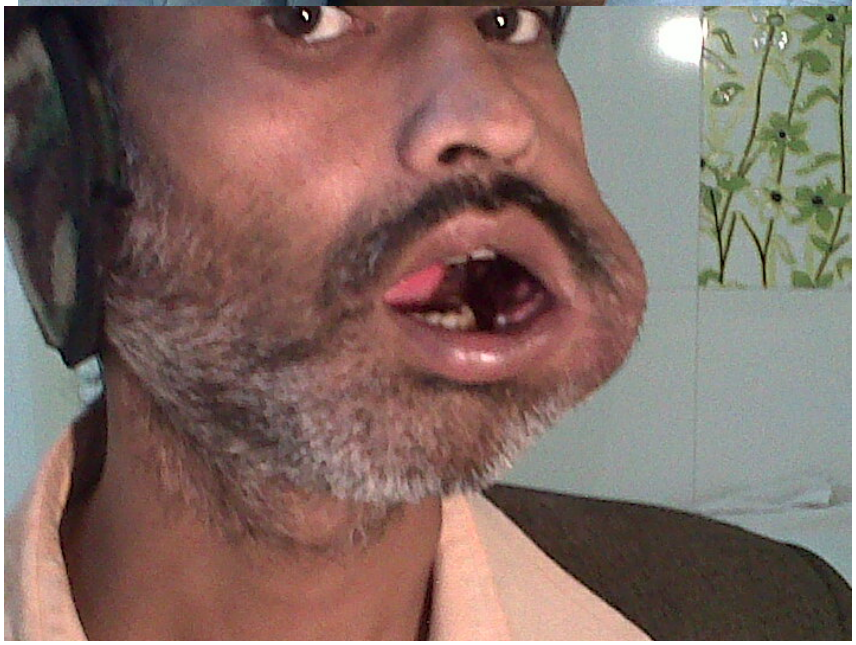
-other poor prognostic factors

positive margins, LVSI, PNI, Node +, ECE

Concurrent Chemo RT

Metastatic Disease Palliation – local, distant sites

Head & Neck Cancers



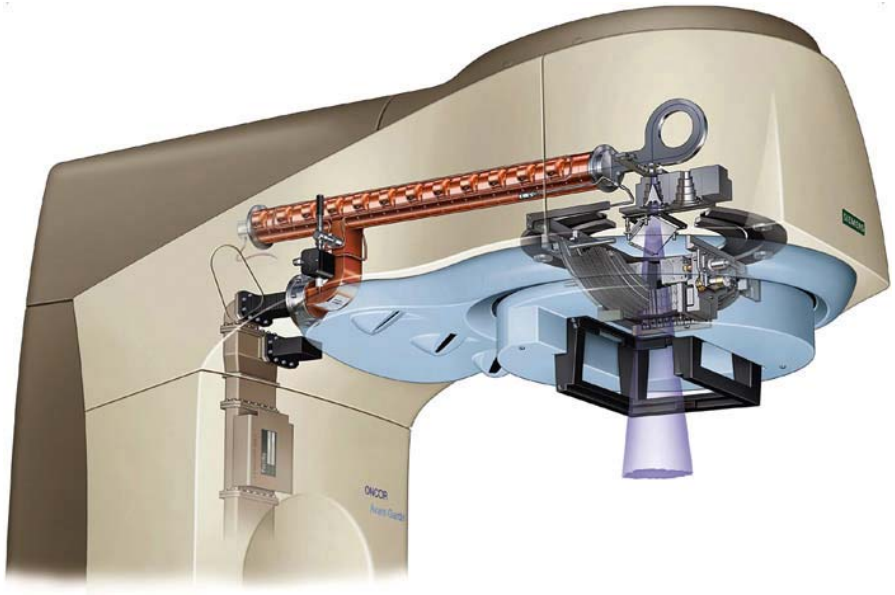
Techniques of Radiation

EBRT
Conventional RT(2D)

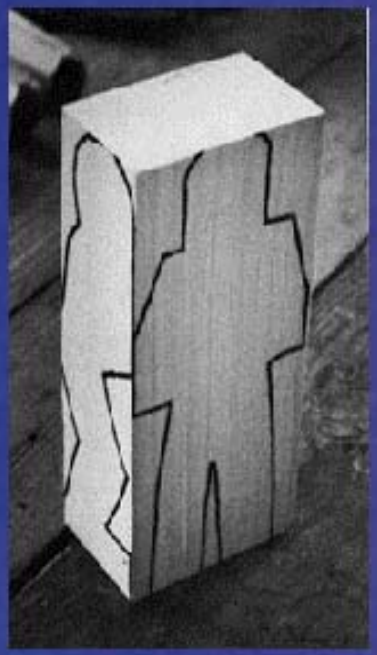
3D CRT
IMRT
IGRT

All forms of Conformal Radiotherapy

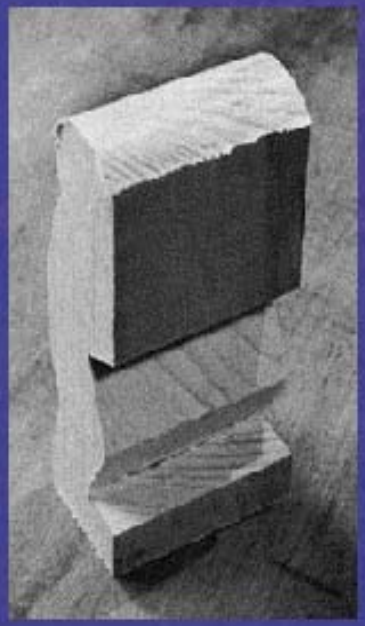
Brachytherapy



Dose Sculpting

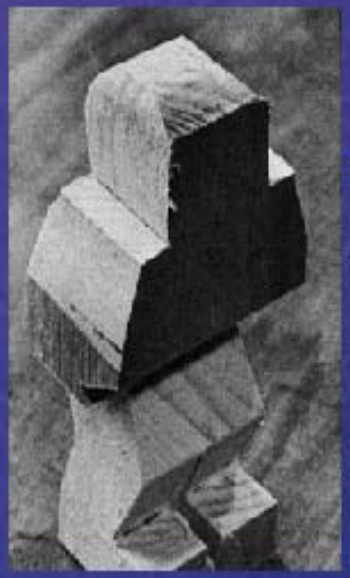


2-D Planning



3-D

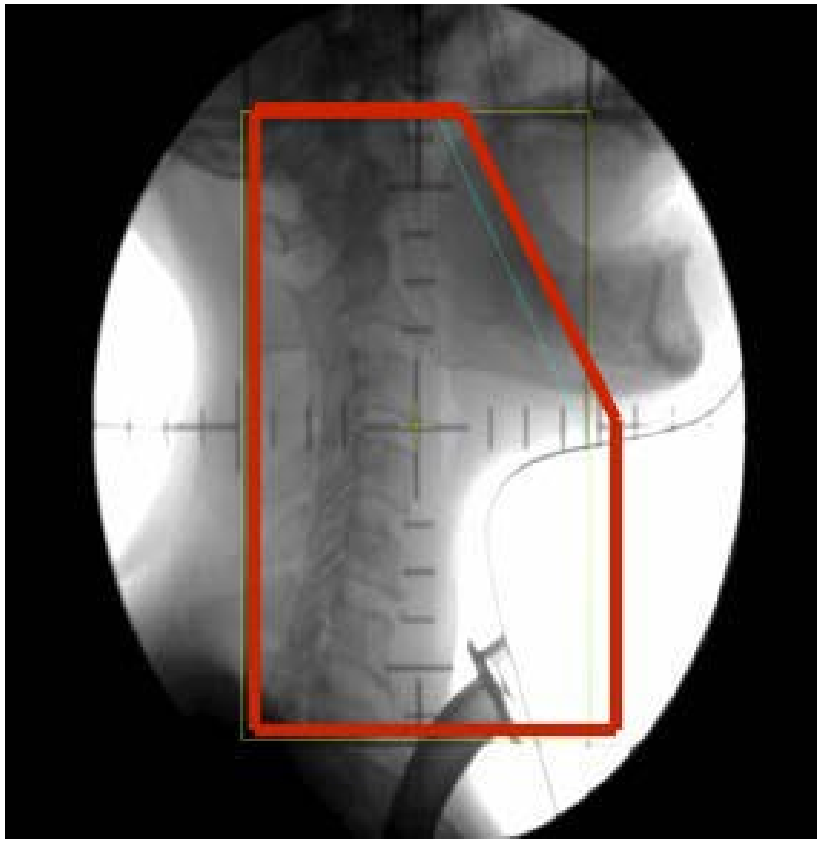
Conformal

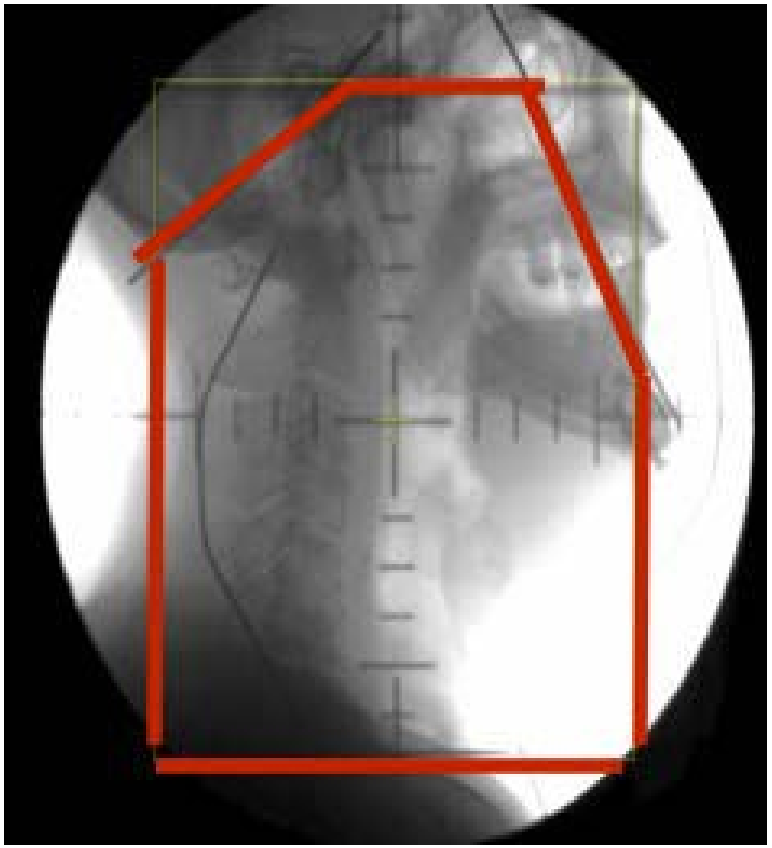


IMRT

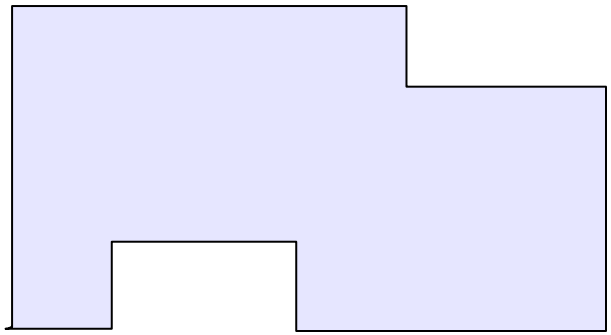
Courtesy of J. Schreiner Kingston Regional Cancer Centre, Ontario

Conventional Radiation fields

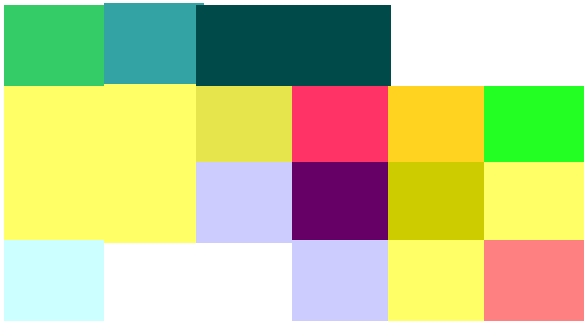




Types of Conformal Radiation



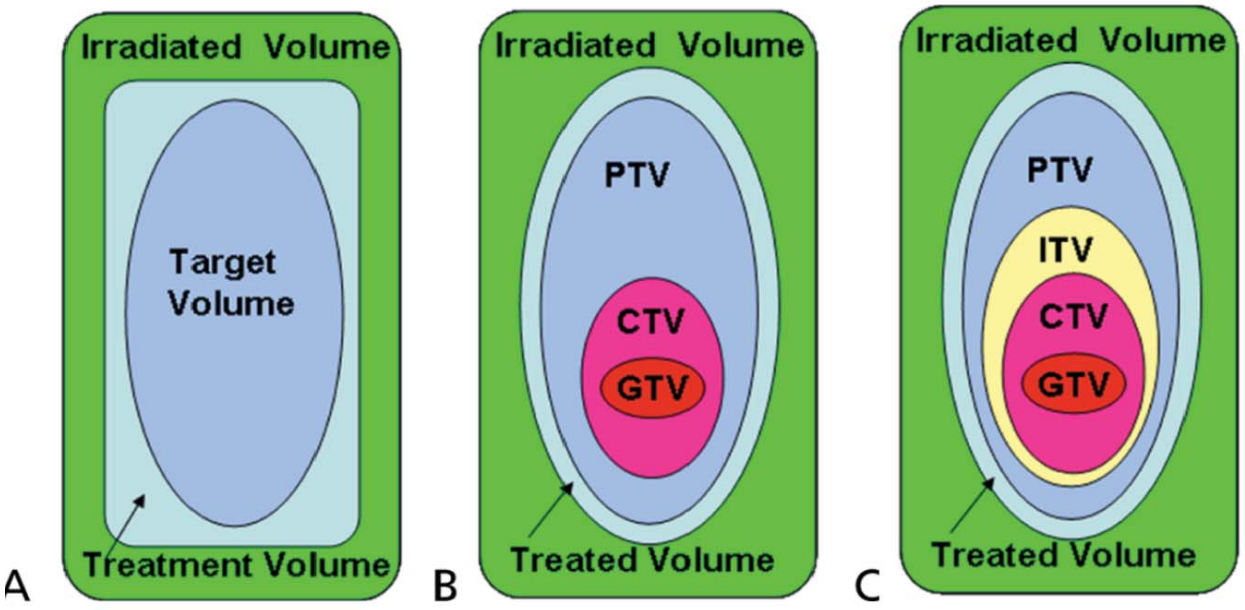
Geometrical Field shaping



Geometrical Field shaping with Intesity Modulation

- Two broad subtypes :
  - Techniques aiming to employ geometric field shaping alone (3D-CRT)
  - Techniques to modulate the intensity of fluence across the geometrically-shaped field (IMRT)

Concepts of Volume



Volumes defined by **International Commission on Radiation Units and Measures (ICRU)** Report : gross tumor volume (GTV), clinical target volume (CTV), planning target volume (PTV), treated volume, and irradiated volume

External beam radiation therapy

3D Conformal RT(3D-CRT)

In 3D-CRT, the anatomic relationship between the patient's tumor and normal anatomy is used to deliver a radiation dose that

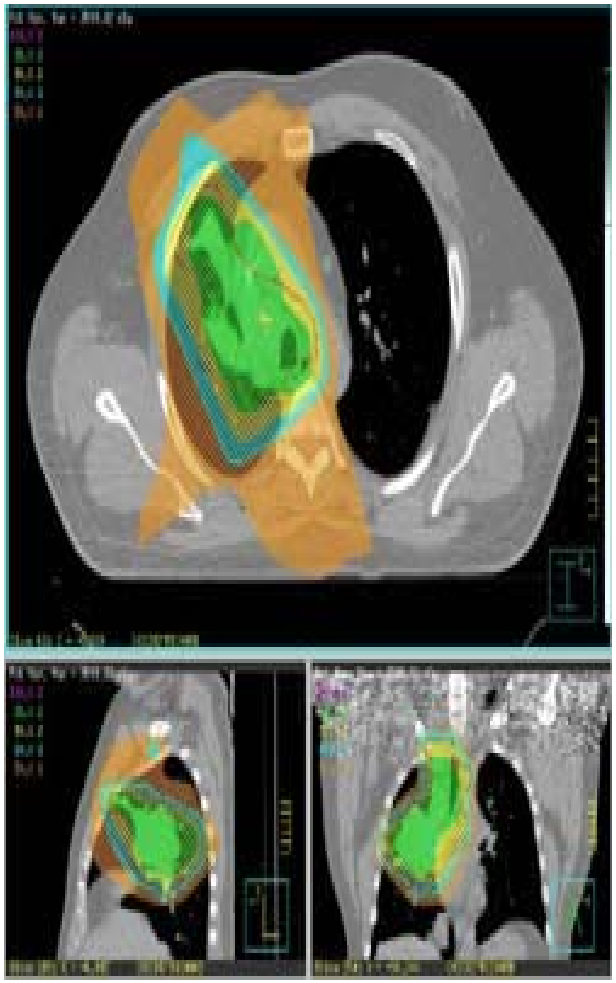
a)conforms to the target volume

b)minimizes exposure to normal structures

•3D-CRT requires a precise definition of anatomy

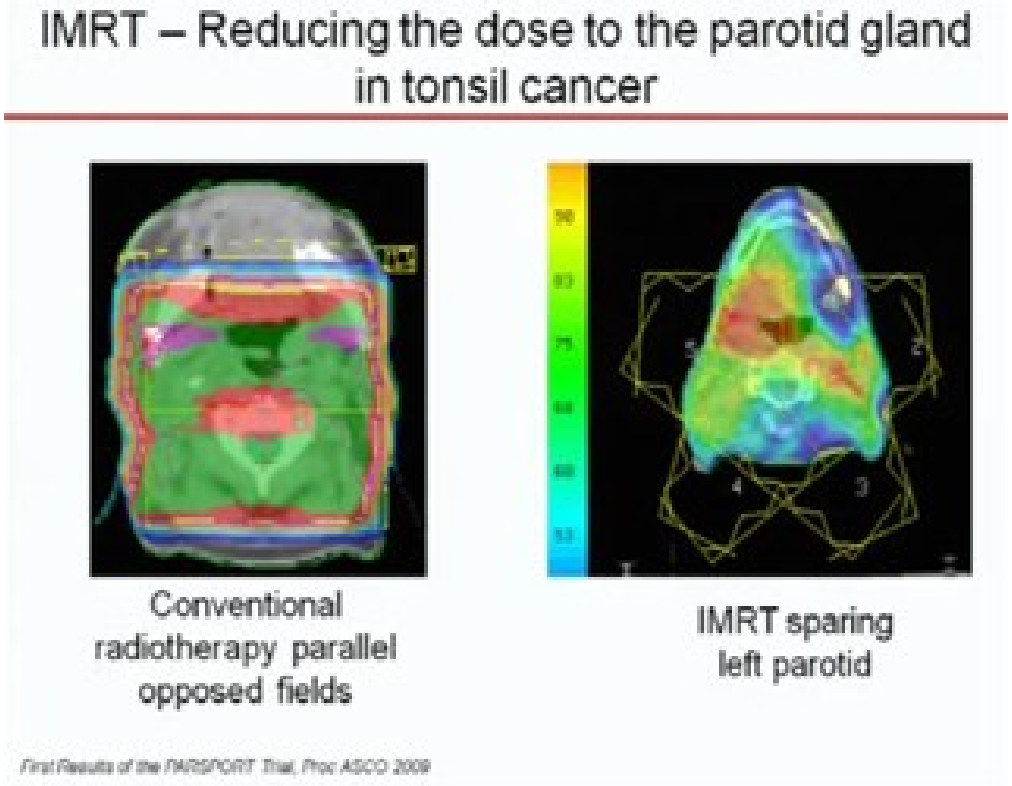
•A sophisticated treatment planning system that can calculate the dose in three dimensions

• A treatment device that can deliver the specified dose



Intensity-Modulated RT

- IMRT, an advanced form of 3D-CRT
- IMRT uses non-uniform radiation beam intensities to maximize the delivery of radiation to the planned target volume while minimizing irradiation of normal tissue outside the target



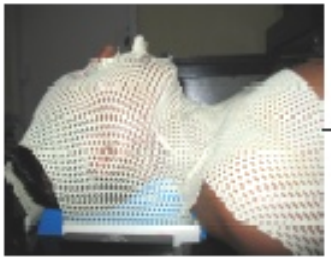
IMRT - Benefits

- Better Normal Tissue sparing
  - Reduced late toxicities
- Dose escalation
- Dose painting
  - Ability to increase dose to areas of higher tumor burden as per biological imaging information
- Re-irradiation

Image-guided RT

- Image-guided RT (IGRT) is a technique that complements IMRT
- Pretreatment imaging on a daily basis which allows for reduction of the margins needed to ensure that the target is accurately treated despite daily tumor motion and setup errors

WORKFLOW OF CONFORMAL RT



Patient positioning and Immobilization

Volumetric Data acqusition

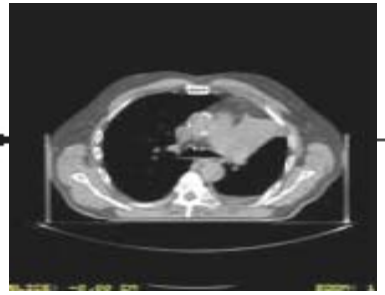
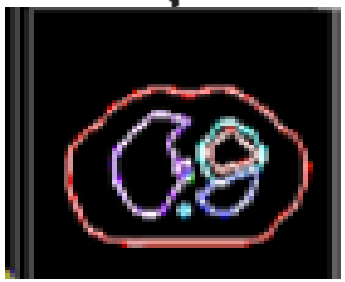
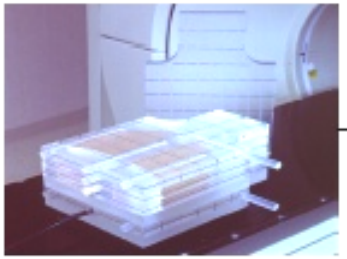


Image Transfer to the TPS

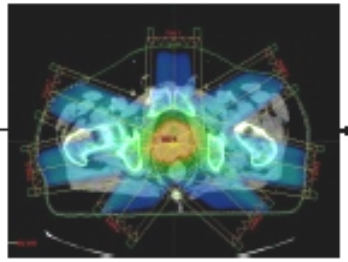


Target Volume Delineation



Treatment QA

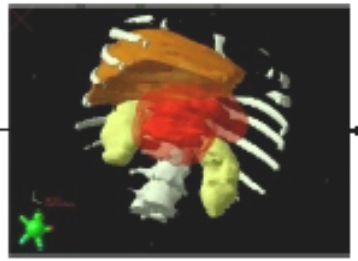
Treatment Delivery



Dose distribution Analysis

Forward Planning

Inverse Planning

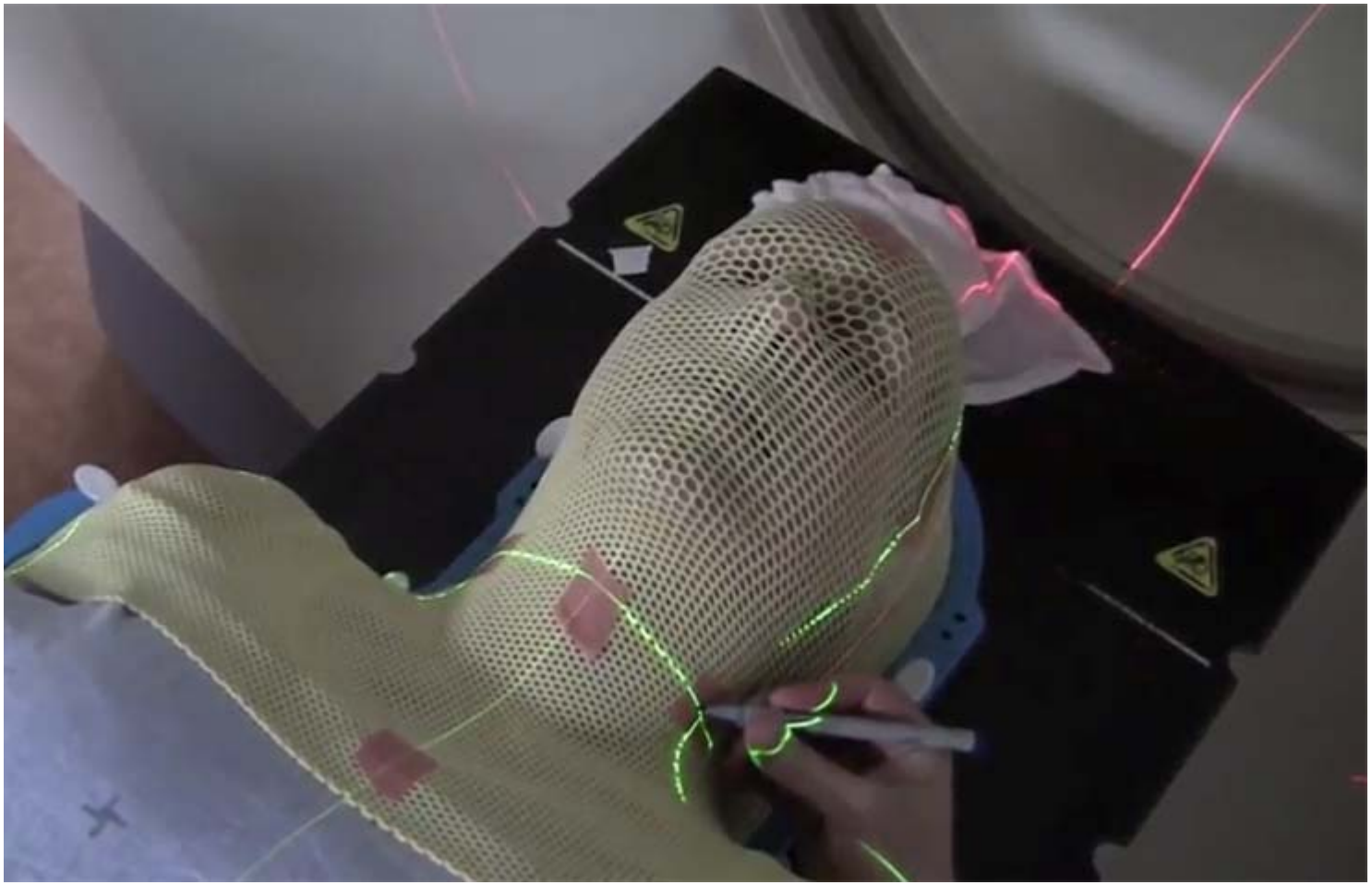


3D Model generation

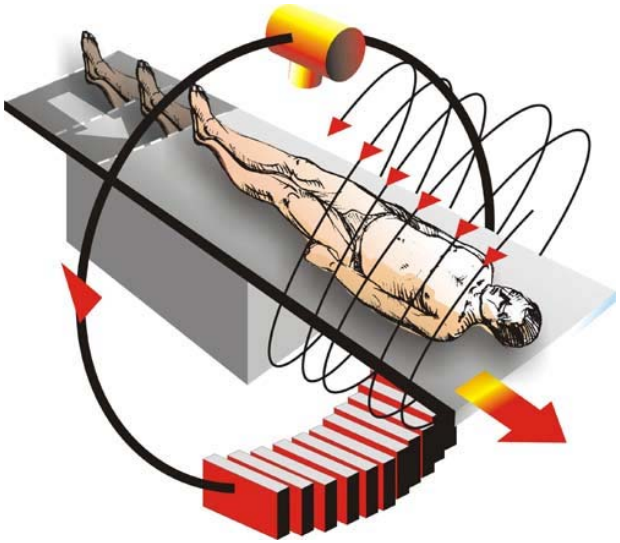
Simulation

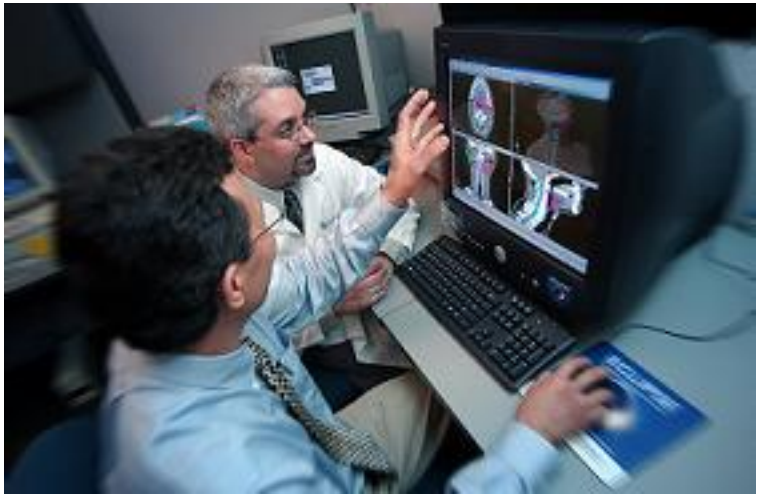
A *face mask* is usually made to hold the head still and allow the targeting markings to be painted on the mask

Marking during CT



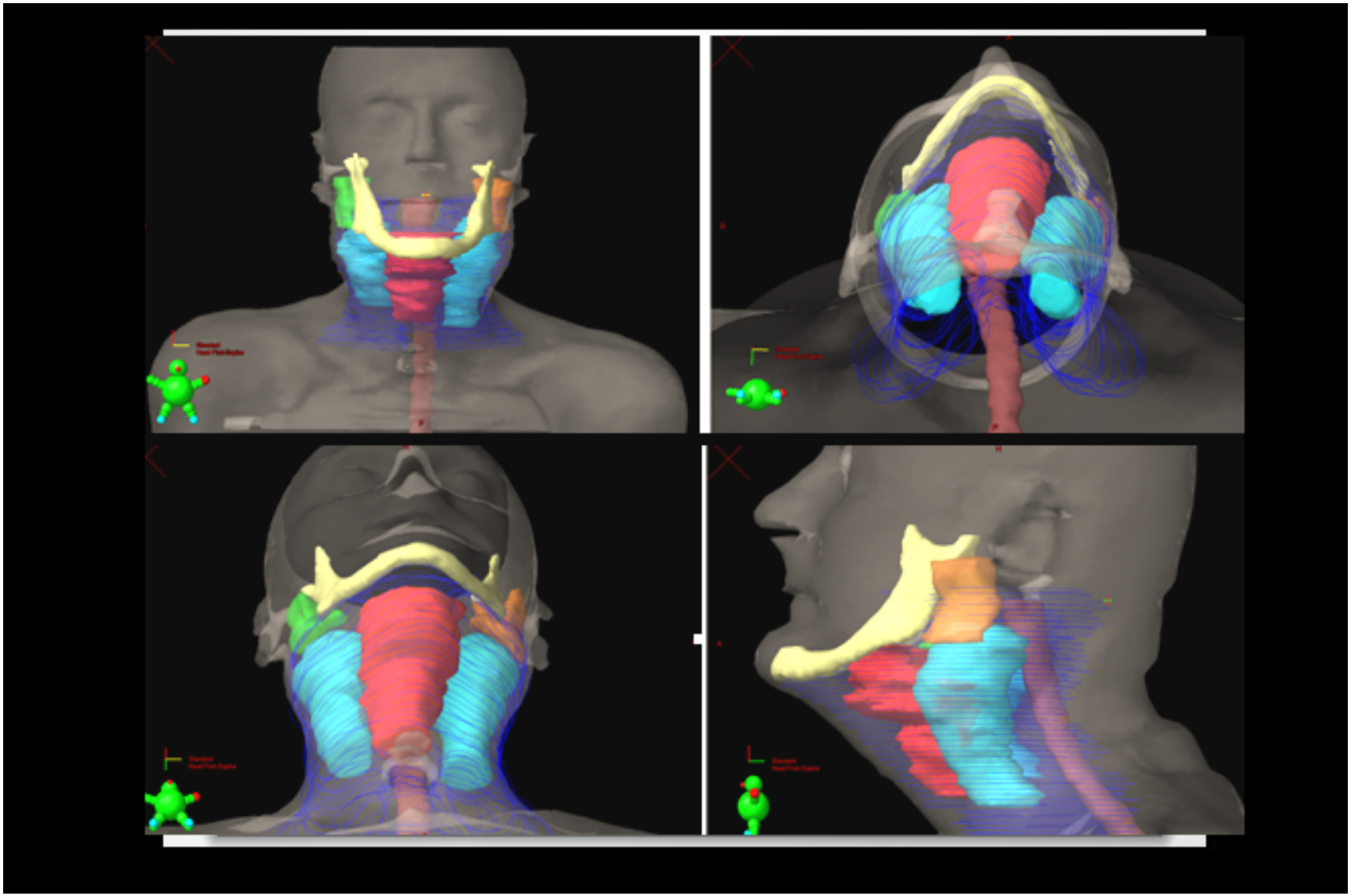
CT scan is obtained at this time





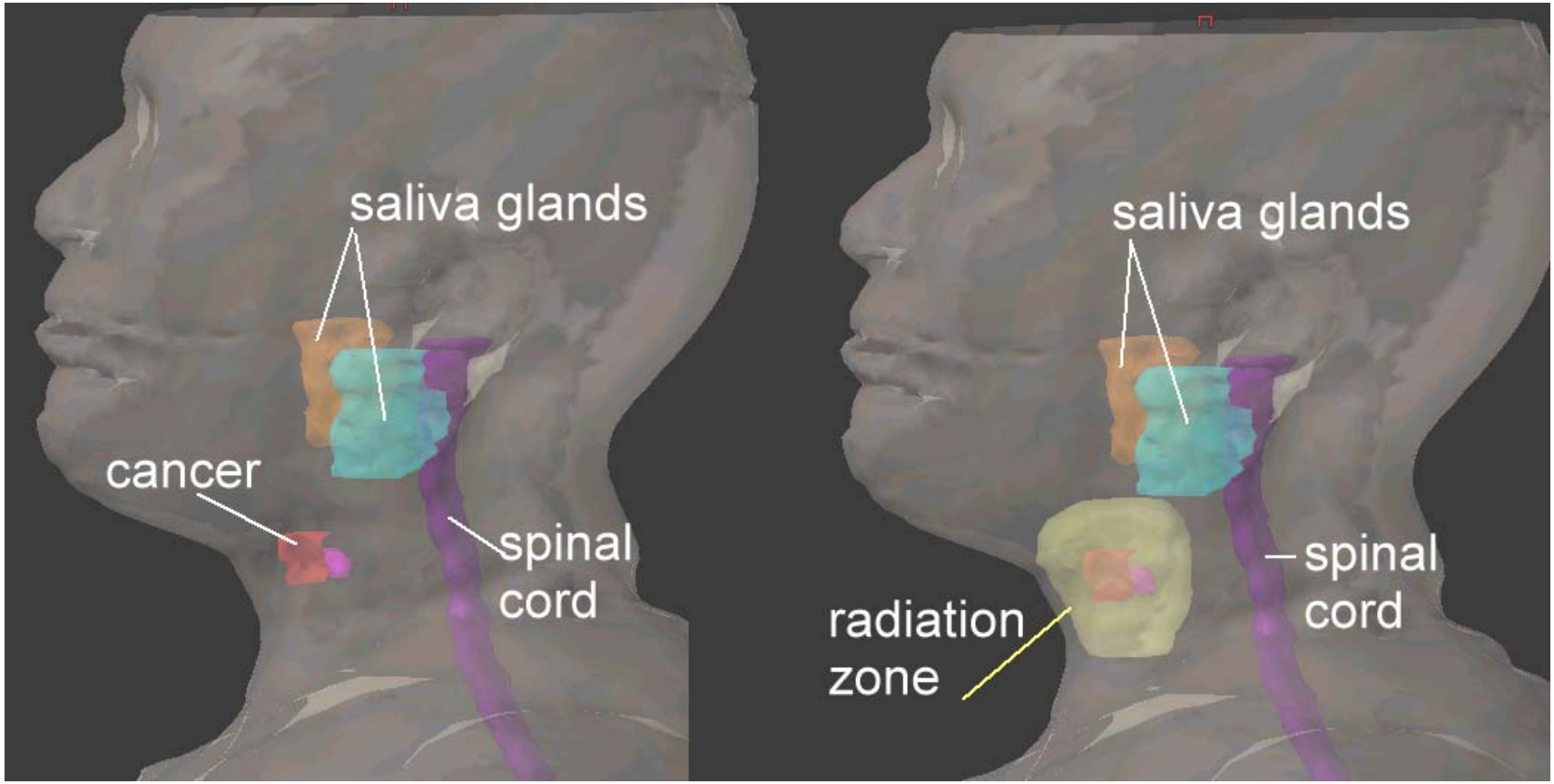
CT images are then imported into the treatment planning computer

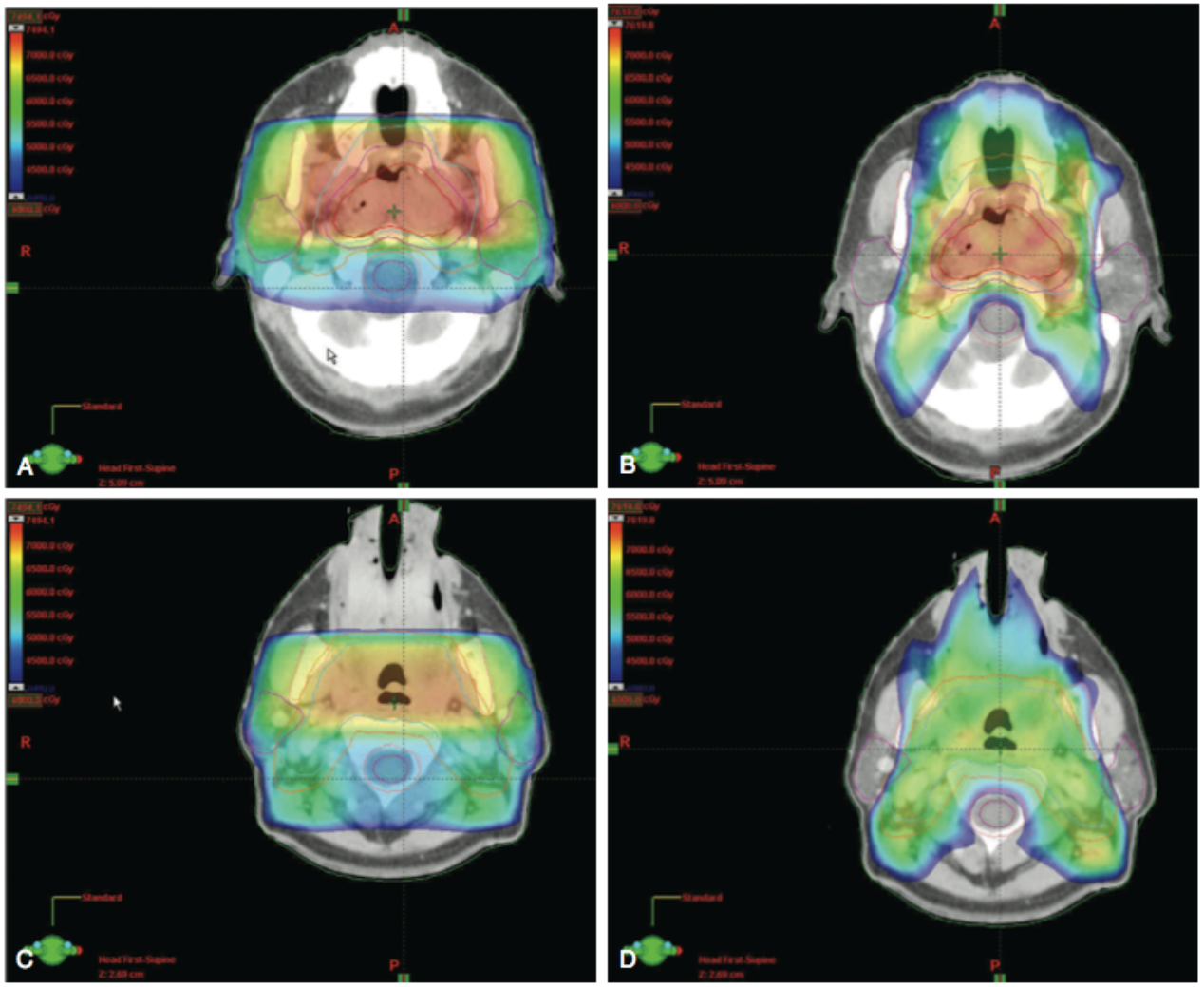
CONTOURING & TARGET VOL DELINEATION



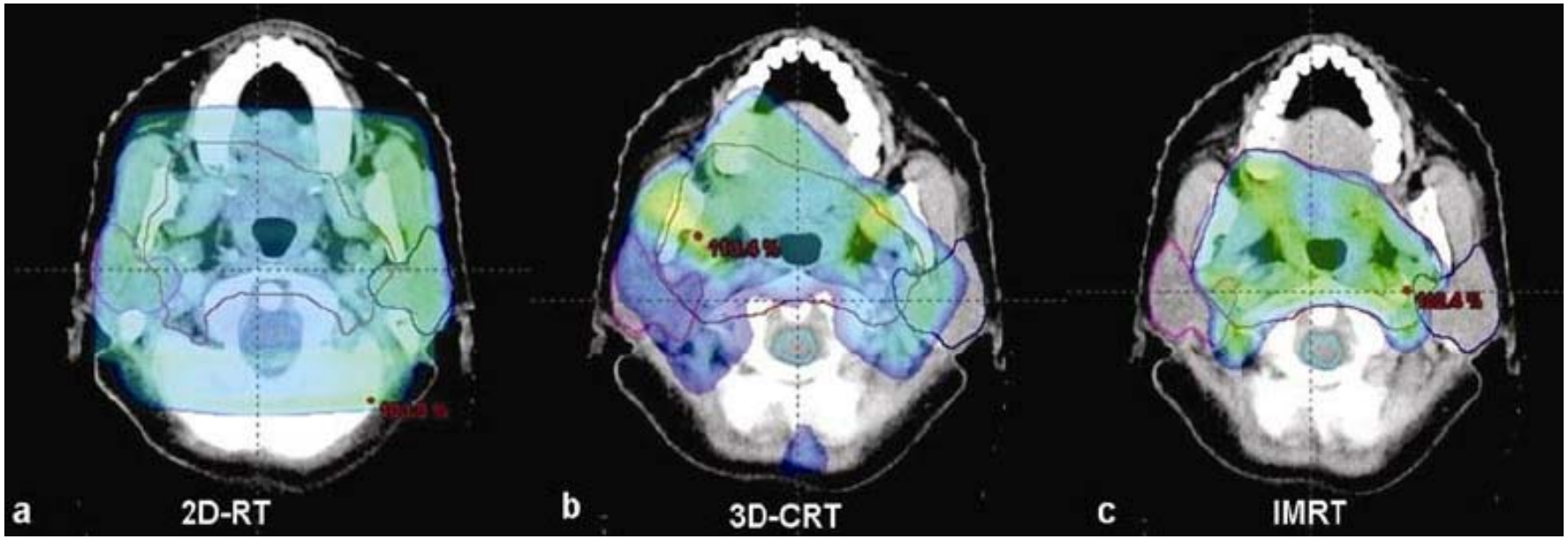
CT and PET scan images are used to create a computer reconstruction of the patient, tumor & normal tissues

For small cancers in the vocal cords it is possible to keep the radiation far away from other normal structures

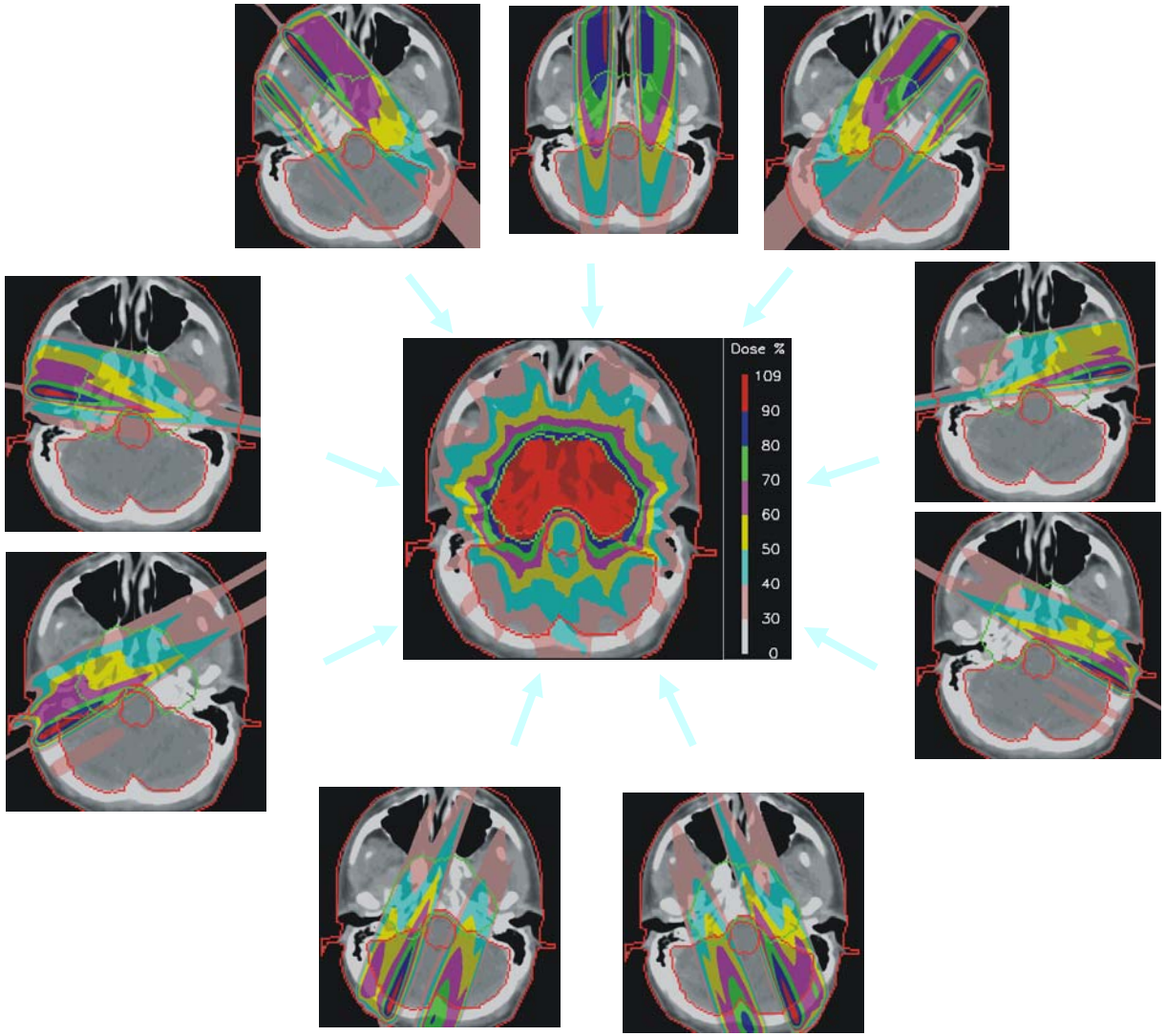




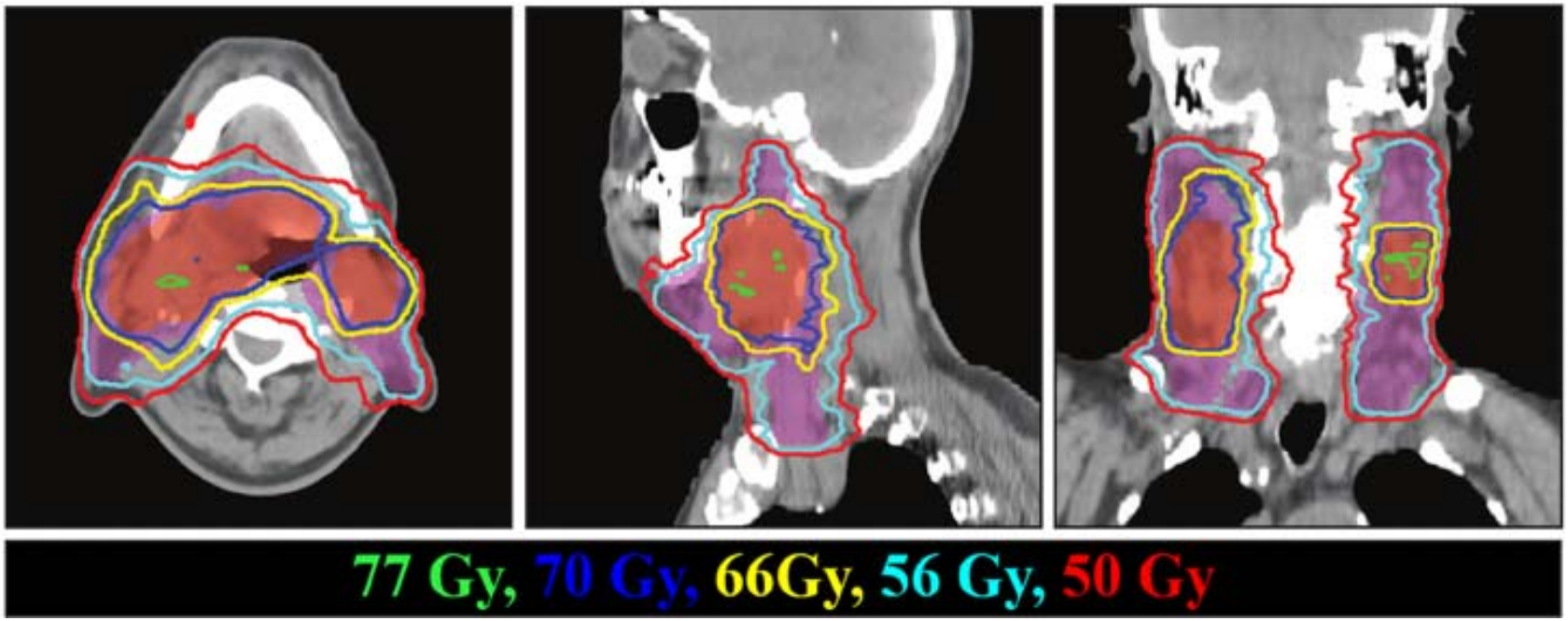
Dose colorwash comparison of coverage on a representative patient with stage T2bN0M0 nasopharyngeal cancer treated in the RTOG 0225 IMRT vs Conventional RT



Axial planning CT slice showing typical dose-wash of (a) conventional radiotherapy (2D-RT); (b) 3D-CRT; and (c) IMRT plan for head-neck cancer.
Note the progressive high-dose conformation to the target volume and sparing of surrounding normal structures

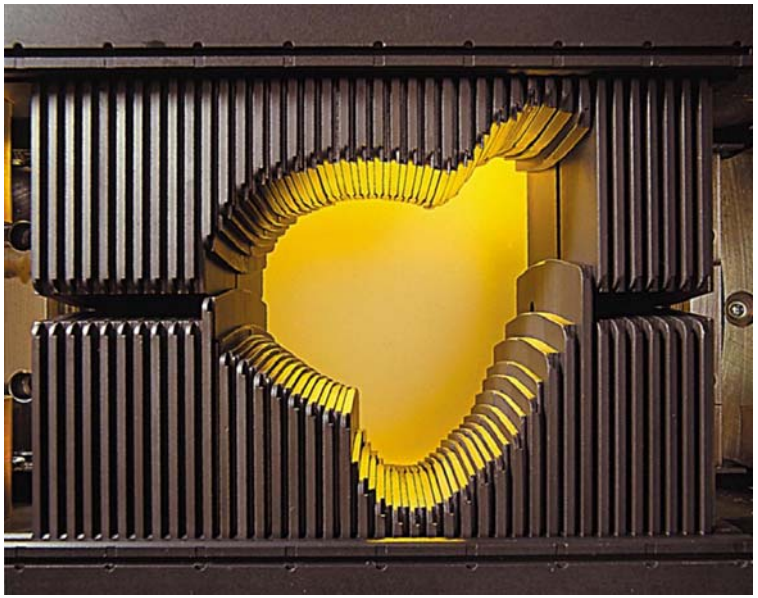


Intensity Modulated Radiation Therapy (IMRT) with 9 x-ray beams

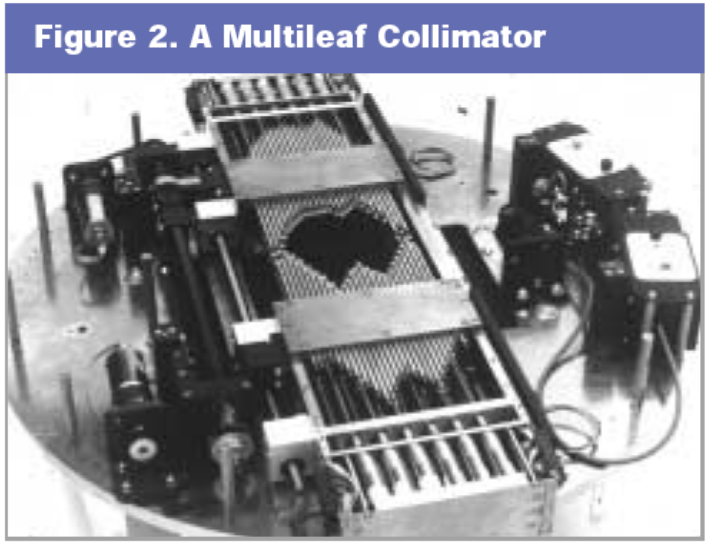


Dose distributions in the axial, sagittal and coronal views for a 9-field IMRT plan

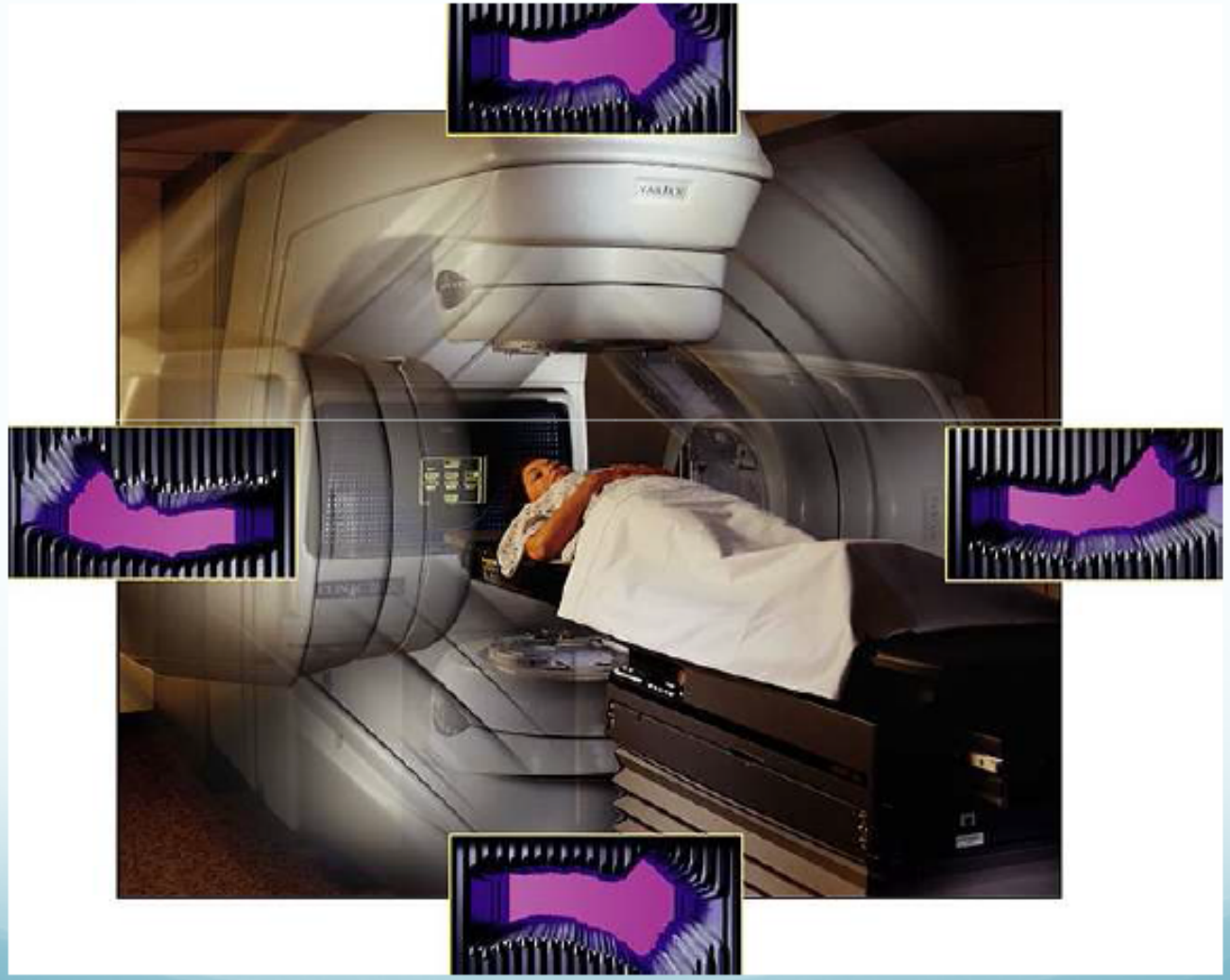
Today: Smart Beam IMRT



- Multi Leaf Collimator is dynamic (computer controlled)
- Up to 120 or more leaves
- Segments shrink to 2.5 X 5 mm
- No patient movement required
- Uses “sliding windows” to speed up treatment (10-15 min) and improve patient comfort
- Makes IMRT efficient, cost effective, quiet

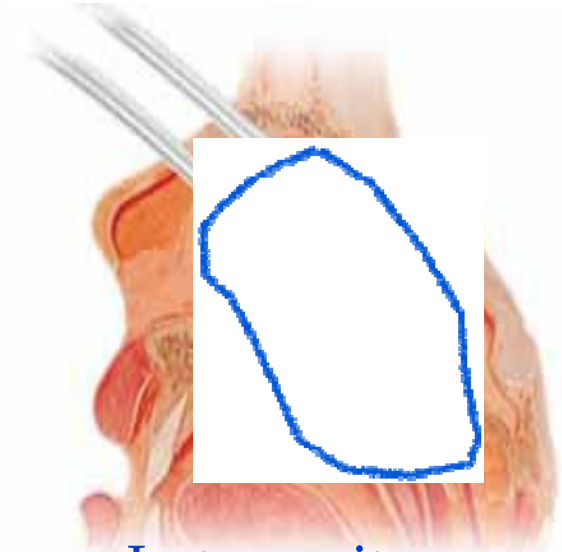


RT Treatment Delivery by Linear Accelerator



MLC

Brachytherapy



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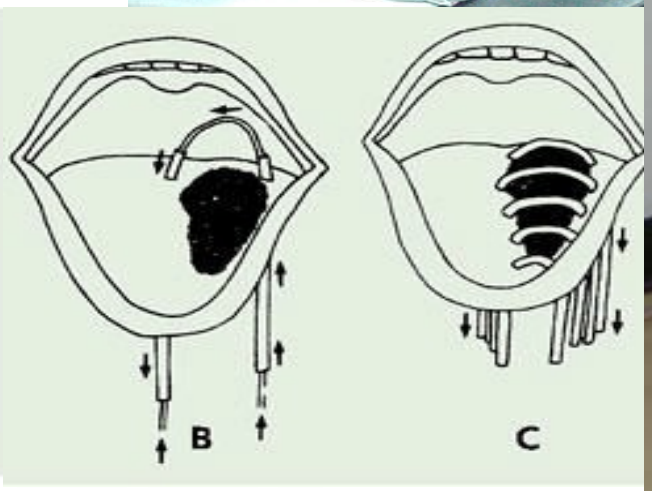

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Brachytherapy

”Brachy" - Greek word *brakhus* - short

•Brachytherapy is a form of internal radiation treatment where radioactive sources are placed on or into cancer tissues/lumen
•Two most common forms of treatment are low dose rate (LDR) & High dose rate (HDR)
•HDR brachytherapy commonly used for H&N cancers

HDR Brachytherapy

- High dose rate (HDR) is a technically advanced form of brachytherapy
- Single source
- A high intensity radiation is delivered with millimeter precision under computer guidance directly into the tumor while avoiding injury to surrounding normal healthy tissue

Brachytherapy for Lip Cancer

Steel Needles Placement

Implant Completed

Treatment

Video of Radiation Treatment


THANK YOU FOR YOUR ATTENTION