

Nasopharyngeal Cancer: Clinical and Research Update

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Disclosures

Clinical Trial Support:

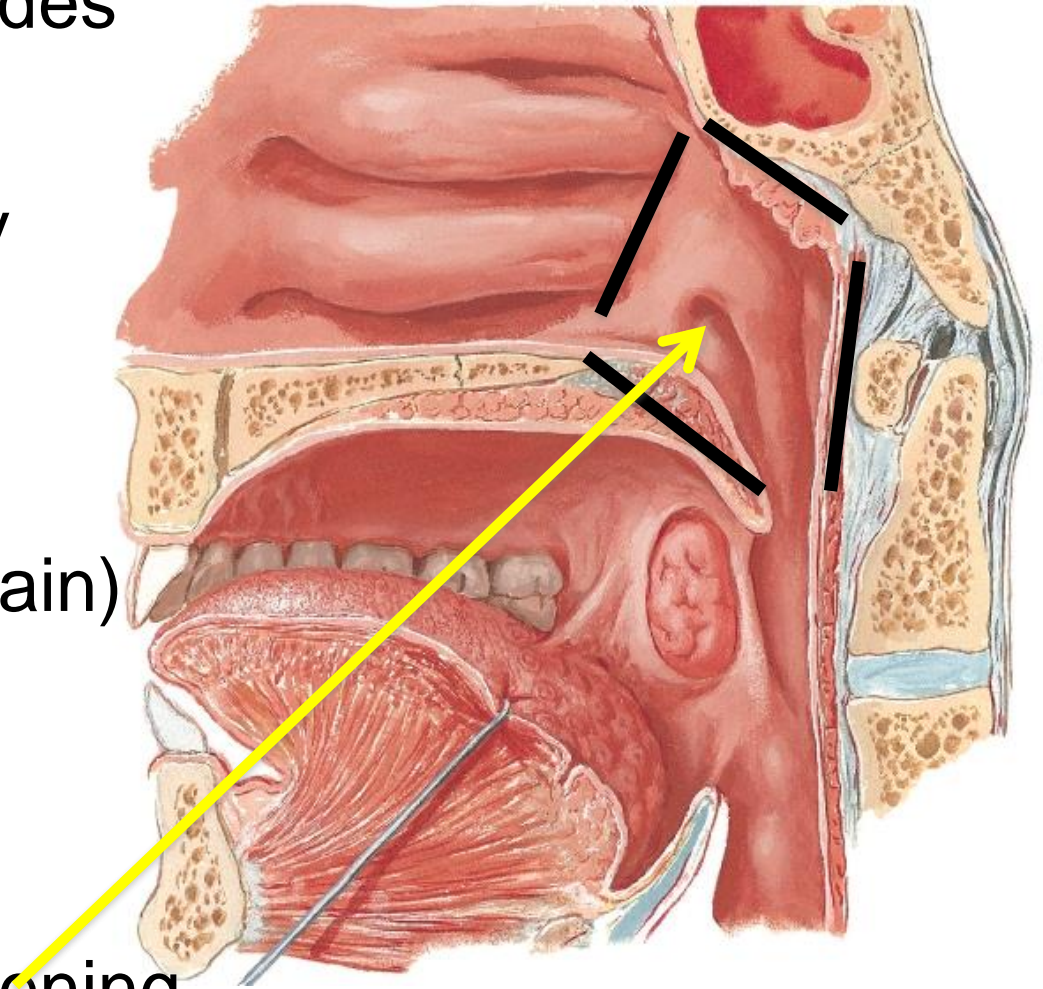
- Genentech
- Bristol-Myers-Squibb (pending)
- Merck (pending)

Honoraria:

- Astra-Zeneca (expert panel)

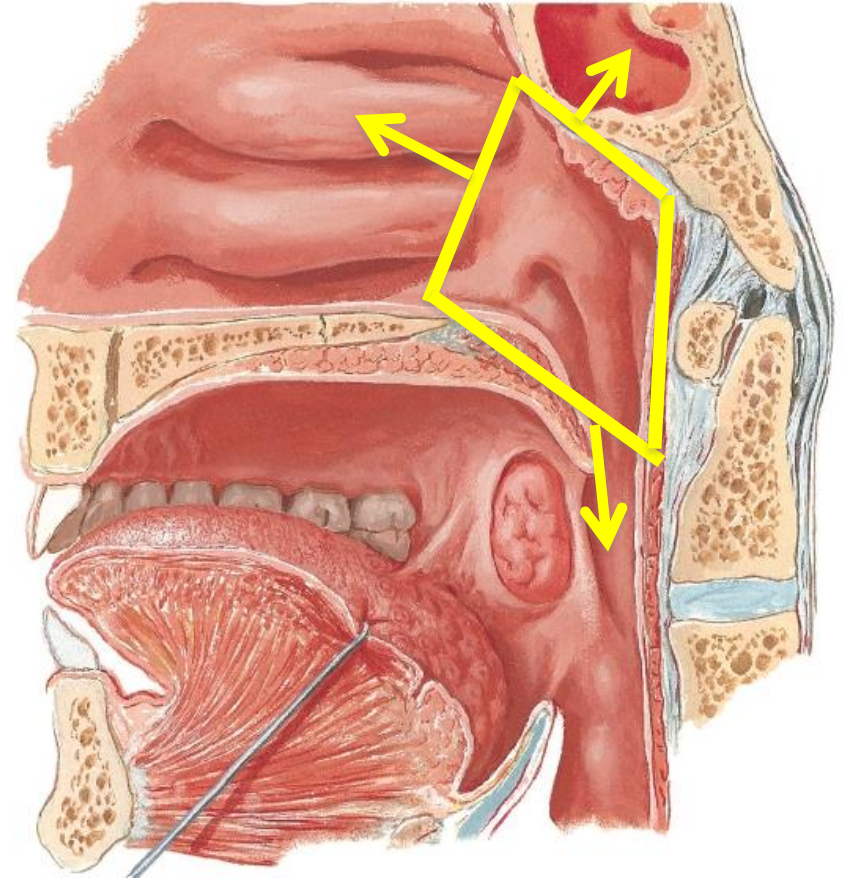
Boundaries of the Nasopharynx

- Like a “cube” with 6 sides
- Front
 - back of nasal cavity
- Back
 - upper spine
- Upper
 - “clivus” (base of brain)
- Lower
 - palate
- Two side walls
 - Eustachian tube opening
 - fossa of Rosenmuller



Spread of Cancer from the Nasopharynx

- Cancer can spread any of the 6 directions
 - Most common:
 - Forward into the nose
 - Down to the throat
 - Into base of skull
 - Sometimes:
 - Further up into brain
 - Rarely:
 - Out of the ears
 - Back into the spine



Nasopharyngeal carcinoma

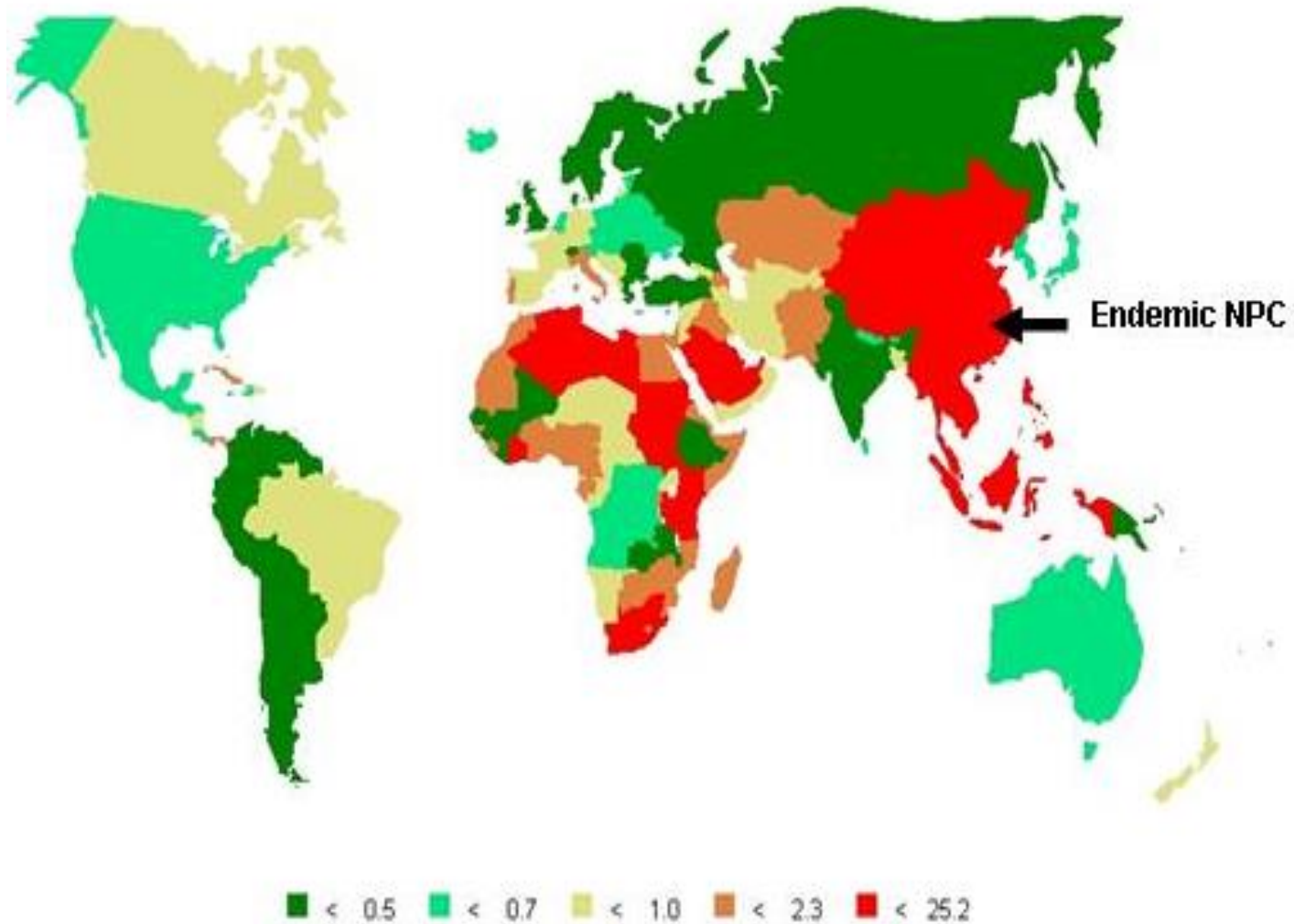
- NPC is rare in Europe and the U.S.
- NPC is extremely common in southern China and Hong Kong, where the rate is 25 times higher than the West (18% of all cancer)
- NPC has been called "the Cantonese cancer"
- NPC is also common in Taiwan, Singapore, Malaysia, Thailand, and Vietnam; also Africa, Mediterranean, and among the Alaska Inuit

Incidence in various countries

- < 1% of all cancers in U.S.
(2/100,000)
- Incidence in Males/100,000/yr:

Hong Kong 28	Alaska 17.2
Connecticut 0.6	Singapore 16.8
Japan 0.4	

Incidence of NPC Worldwide

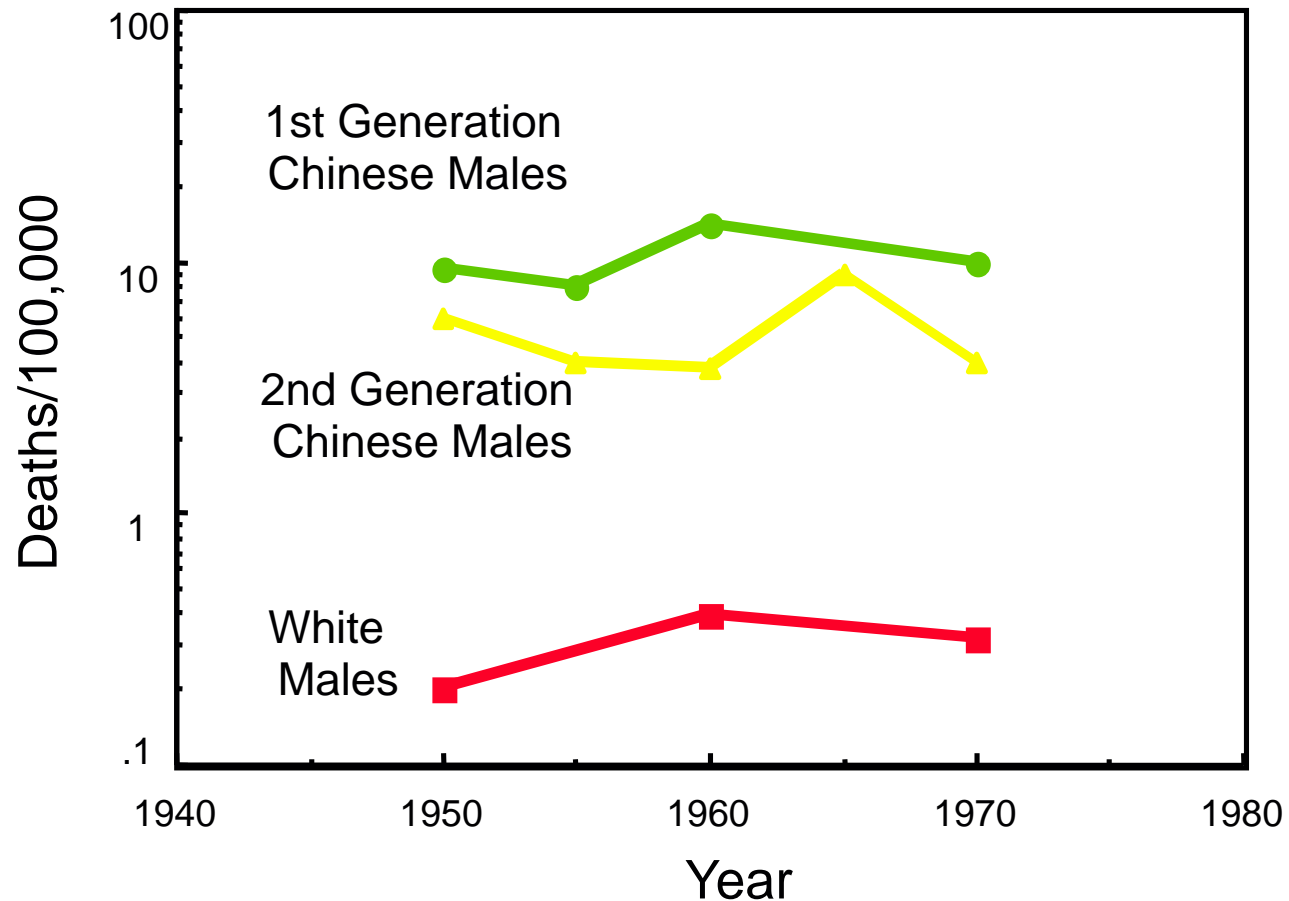


San Francisco Bay Area

- In San Francisco, we have a high proportion of southern Chinese/Hong Kongese immigration
- There is a similar pattern of migration to Southeast Asia, Canada, and Australia
- Usually people are diagnosed with NPC at age 50-60 but they can be very young (teens-20s)
- Siblings or children of NPC patients are at higher risk
- The ethnic predisposition for NPC carries into the second generation after immigration

Age-Standardized Mortality Rates From NPC in California

(P. Buell, Cancer Res. 34:1189-1191, 1974)

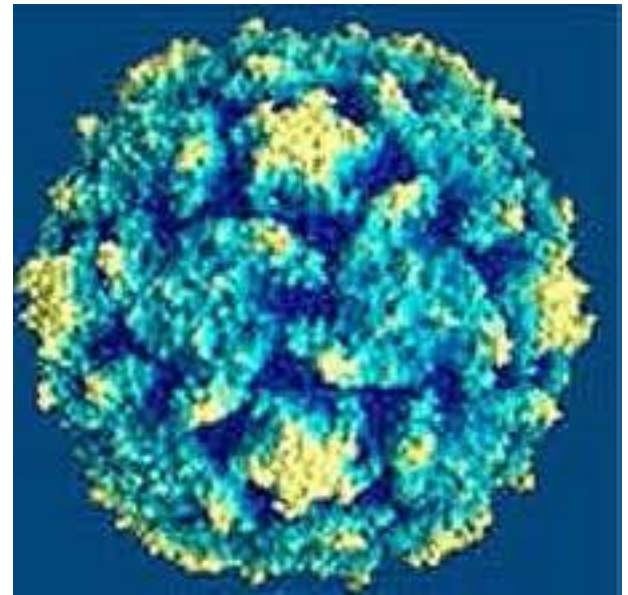


Risk factors

- Smoke from wood fires (polycyclic hydrocarbons)
 - chronic nasal infection, poor hygiene, poor ventilation
- Occupational exposure to dust, smoke, inhalants
- Salted fish (nitrosamines) → RR 5.6
- Smoking, Alcohol
- Formaldehyde
- Radiation exposure
- AND.... GENETICS + EBV....

Role of Epstein Barr Virus (EBV)

- EBV is a common virus
- 95% of people in U.S. are exposed by 30–40 years of age
- The World Health Organization does not have preventative measures because it is so easily spread and is worldwide
- Very rarely does Epstein-Barr virus lead to cancer



Early symptoms of NPC

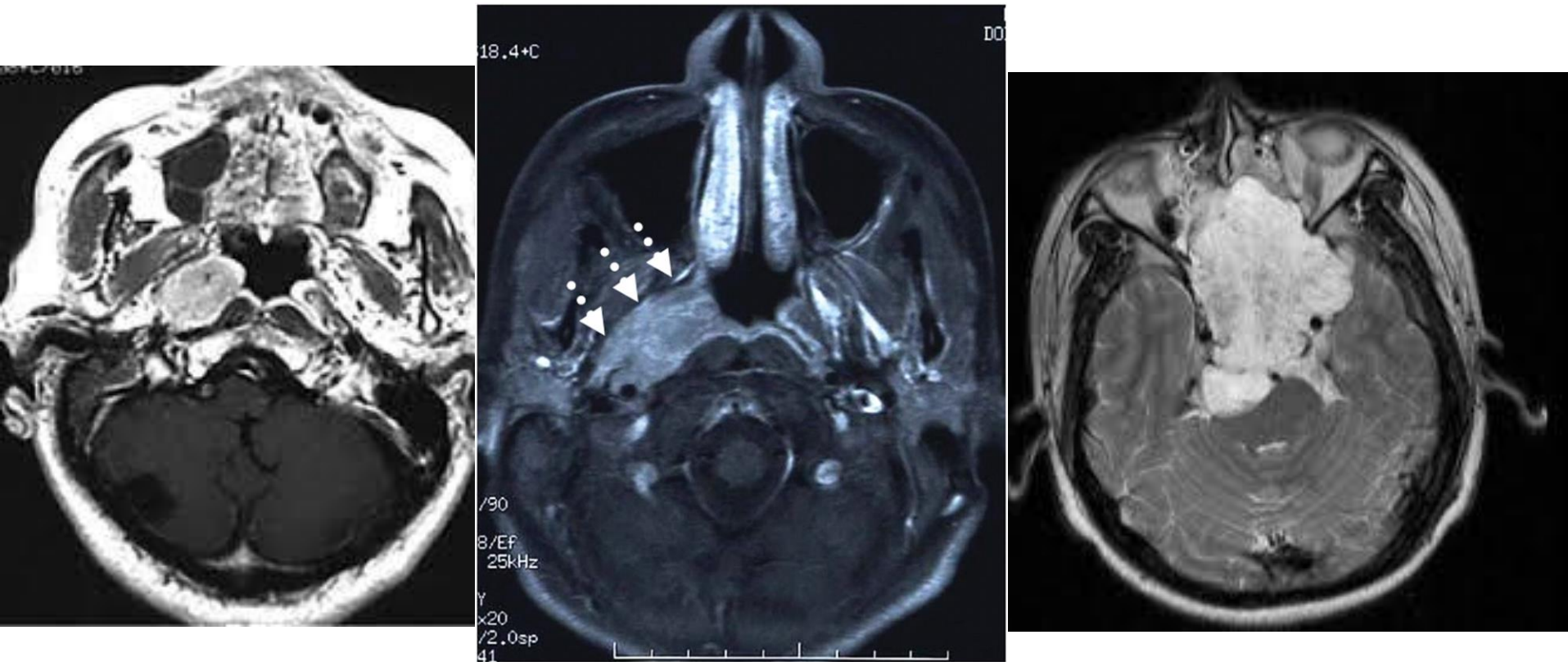
- Lump in the **neck**
- Nasal obstruction or “congestion” or trouble breathing; bleeding from **nose**
- Deep ear pain or “stuffy **ears**” or sudden hearing problem or ringing/buzzing
 - Sore throat/difficulty swallowing
 - Pain in mouth or throat or neck
 - Facial numbness or changes in vision

ENT or OHNS

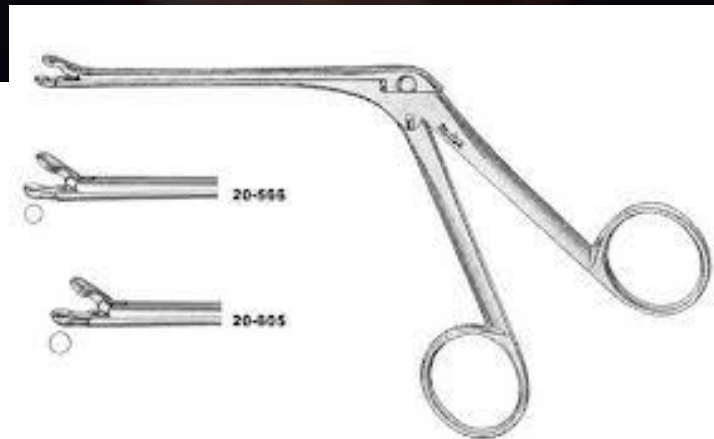
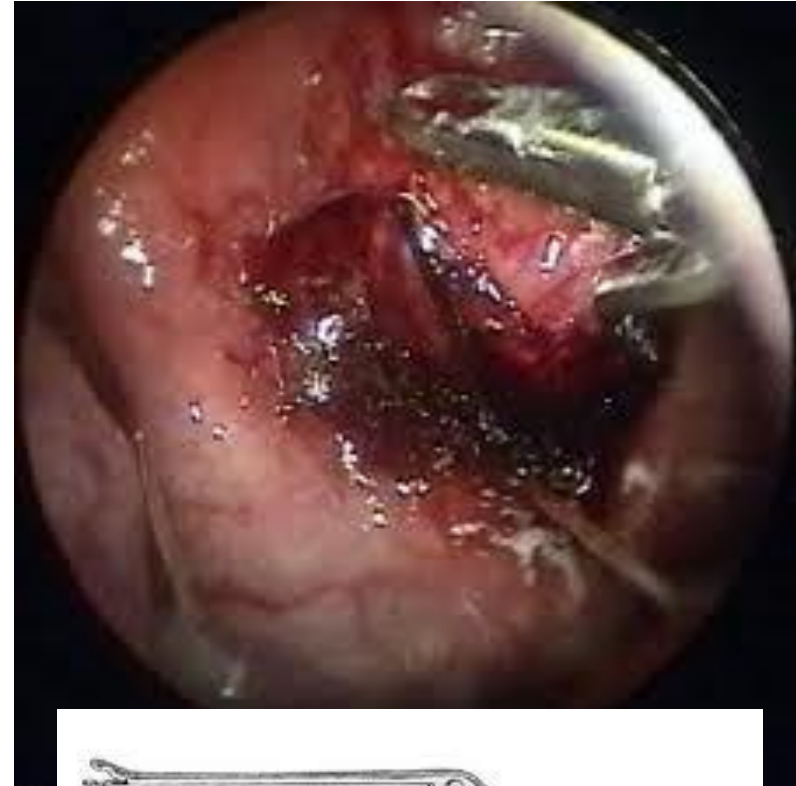
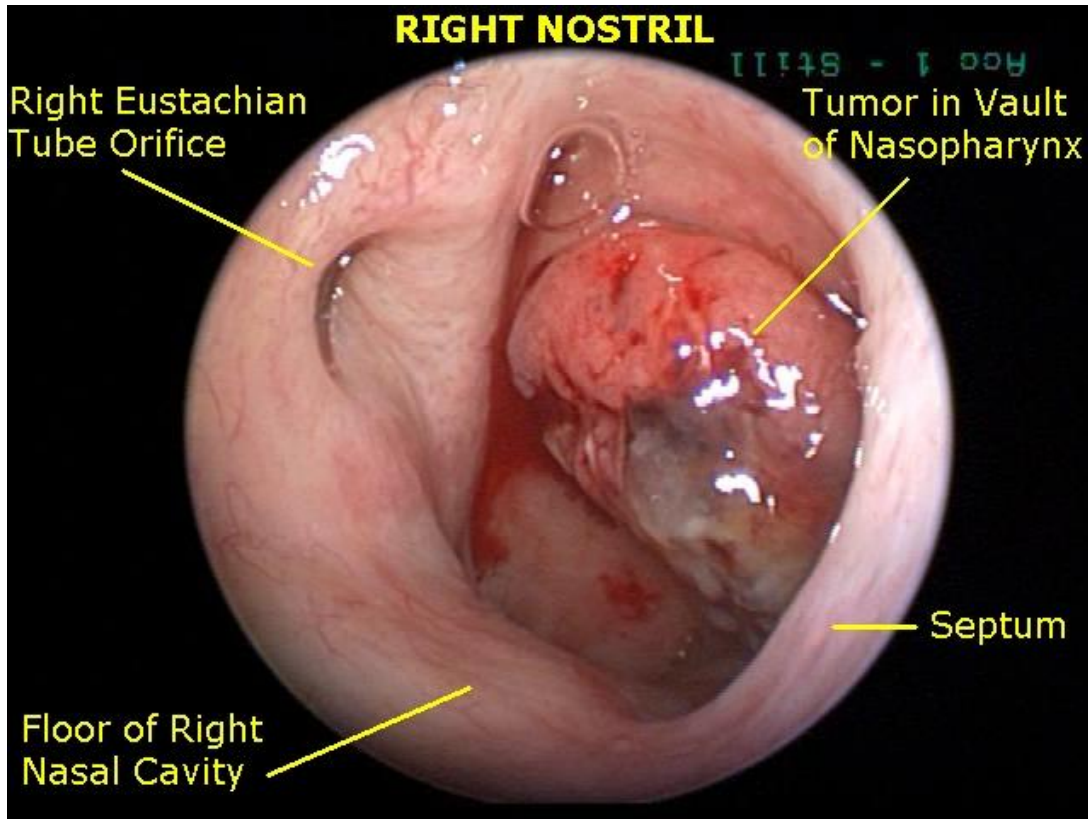
- History and physical examination
 - Examination with nasal endoscopy
- Biopsy of cancer mass: cupped forceps from nose, or thin needle from neck
- MRI or CT scan
- PET/CT
- Bloodwork



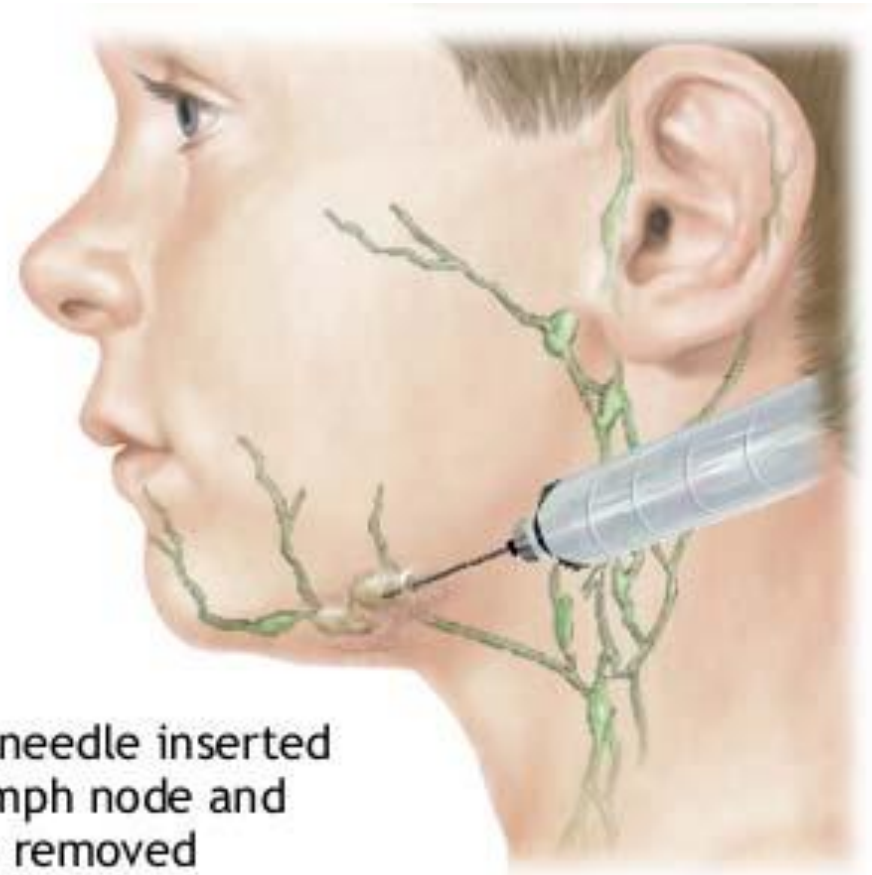
What NPC looks like on MRI scans: early to advanced stage



Biopsy of a nasopharynx mass

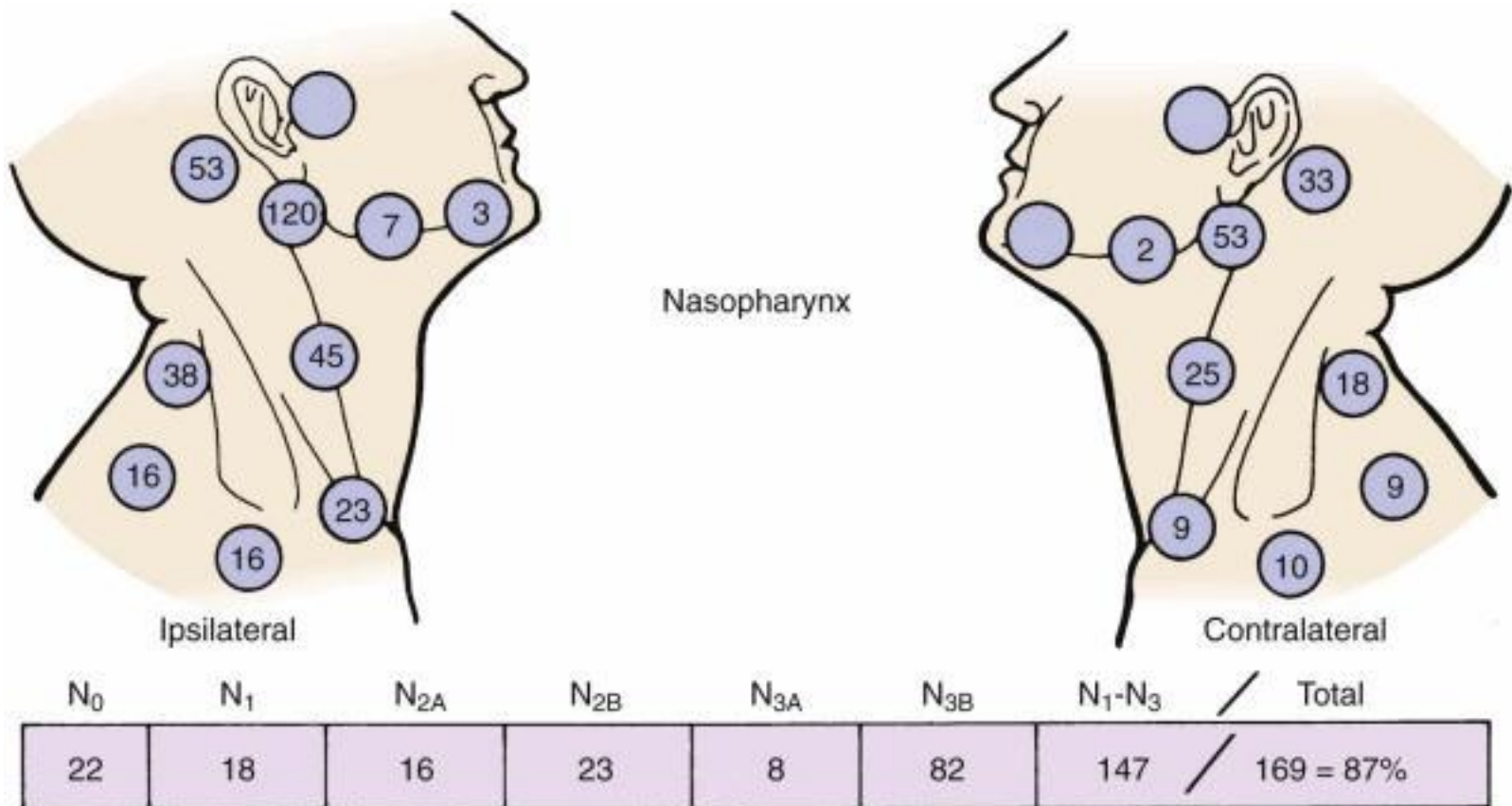


Fine needle aspiration biopsy from enlarged neck node



Biopsy needle inserted into lymph node and sample removed

Spread from nasopharynx to the lymph nodes of the neck



Spread from nasopharynx to the lymph nodes of the neck

- Lymph node involvement at diagnosis
 - 90% have one side of the neck
 - 50% have both sides of the neck
 - This is why we do not recommend surgery (cannot get it all out)
- From lymph nodes, cancer can spread to bones, liver, lungs

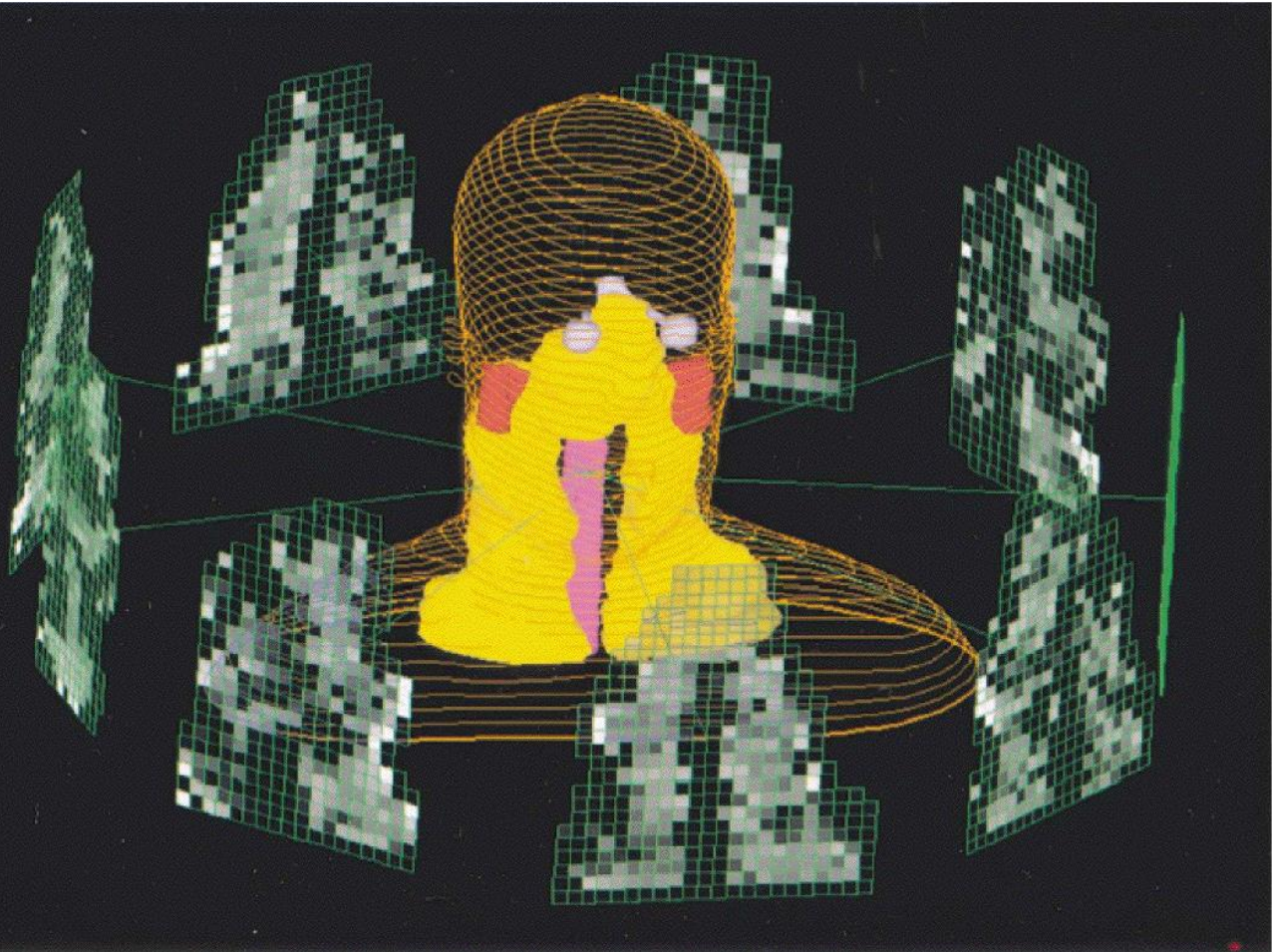
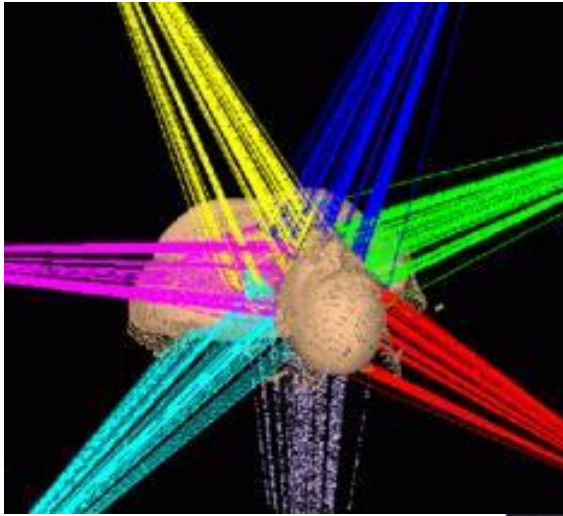
Treatment modalities

- Radiation + chemotherapy
- Chemotherapy is given for another 2-3 months after chemoradiation
- Surgery is only done if nasopharynx or neck that does not respond to chemoradiation
 - Do not start with a neck surgery!
 - Many other cancers of mouth and throat start with surgery – NPC Is unique!

NPC should be treated with intensity modulated radiation therapy (IMRT)

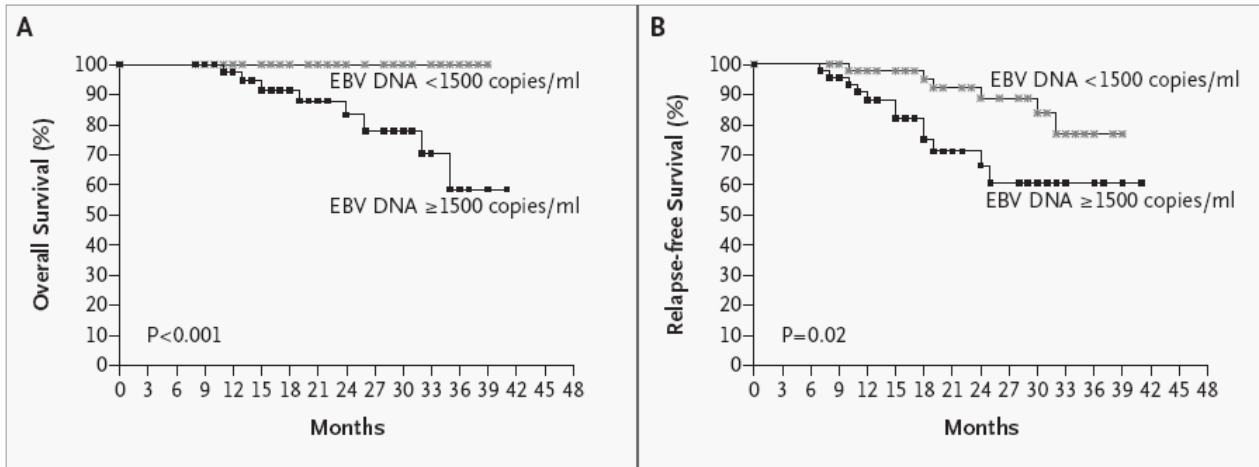


IMRT shapes the radiation from many angles → combining all of the shapes avoids the eyes and brain

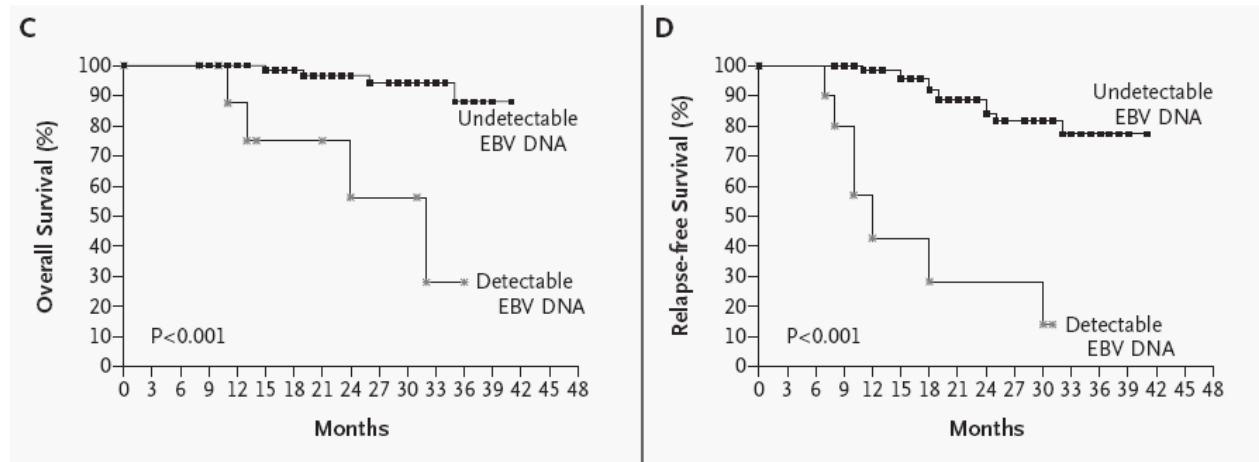


High levels of Epstein Barr Virus in the blood predicts the outcome of the treatment

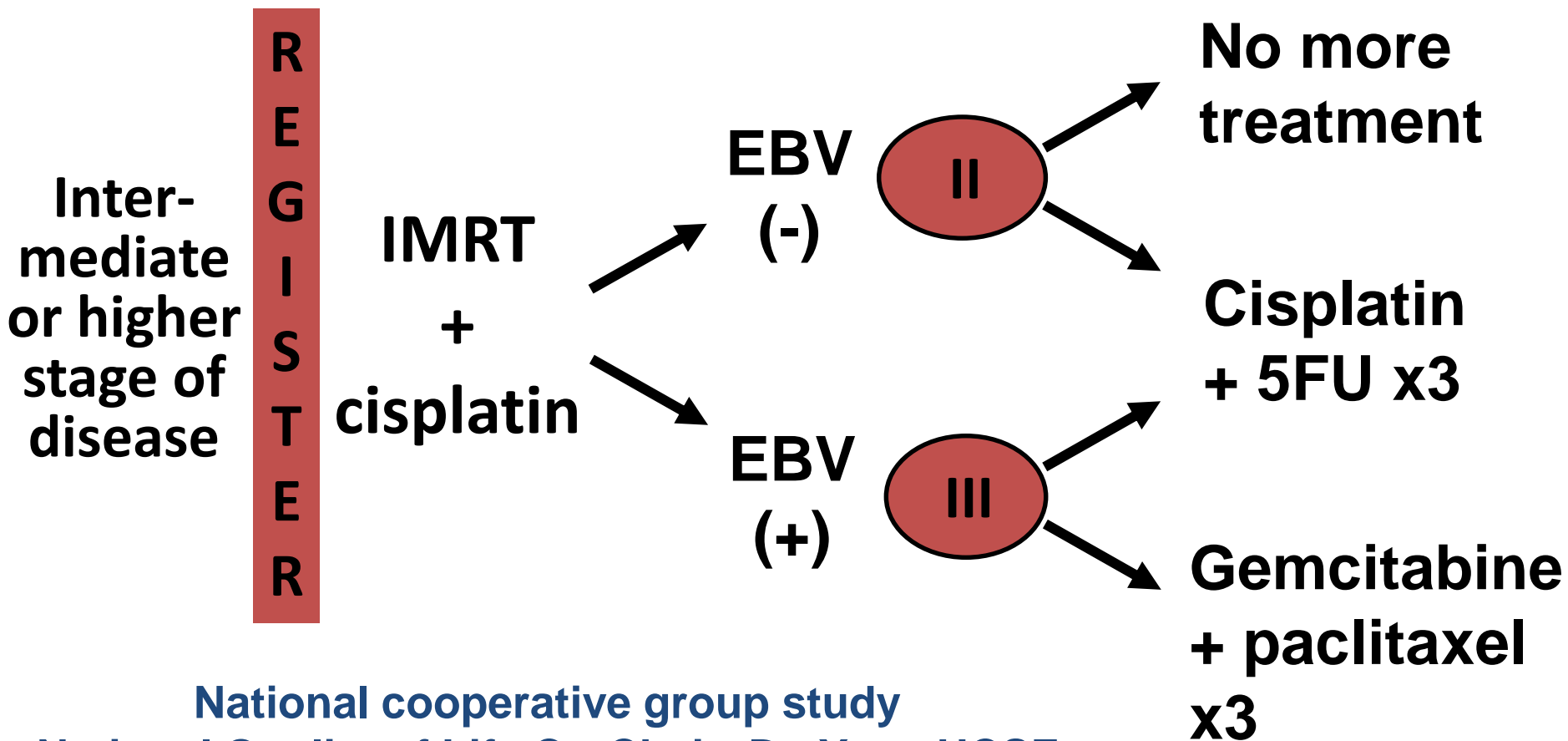
Pretreatment



1 week after RT completion

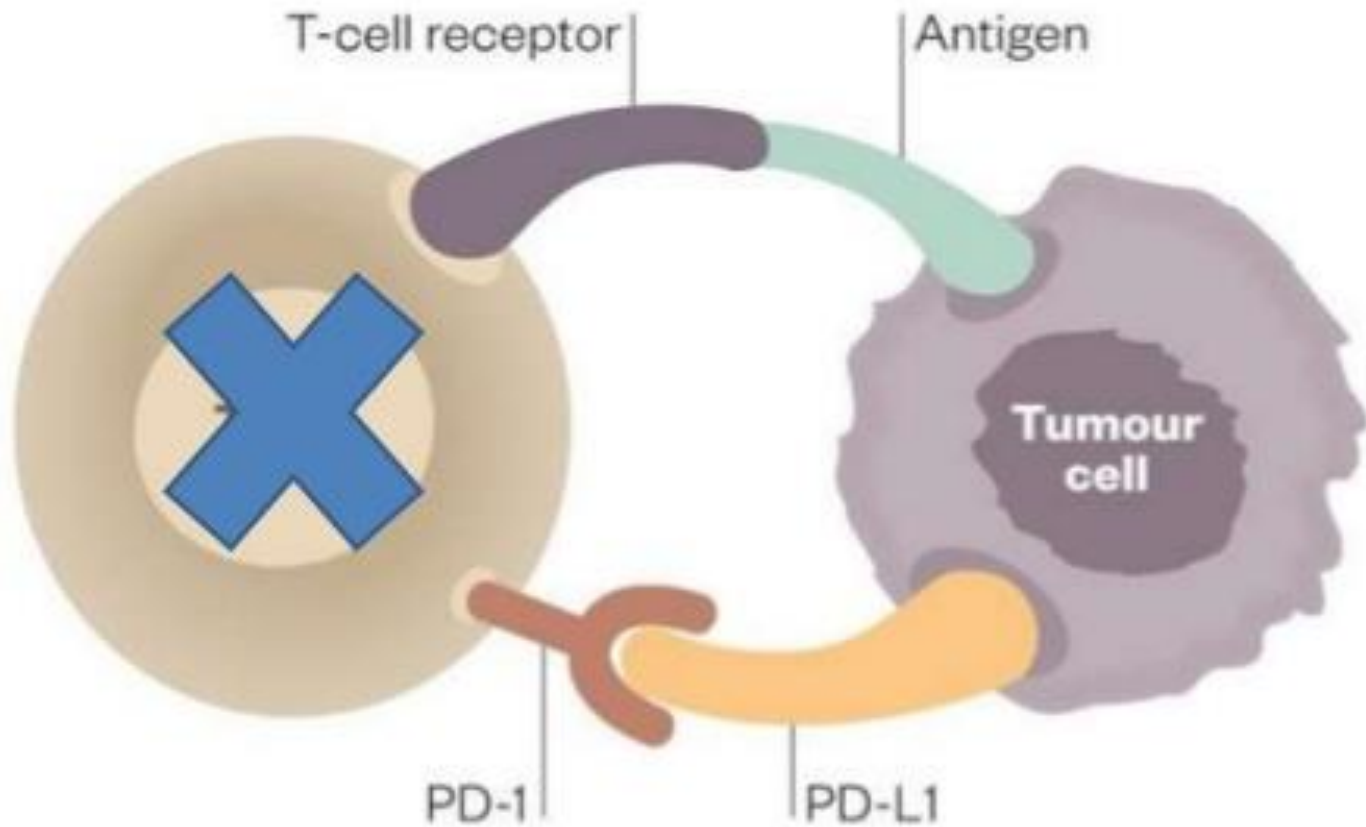


NRG-HN001: National EBV Testing Study for Newly Diagnosed NPC

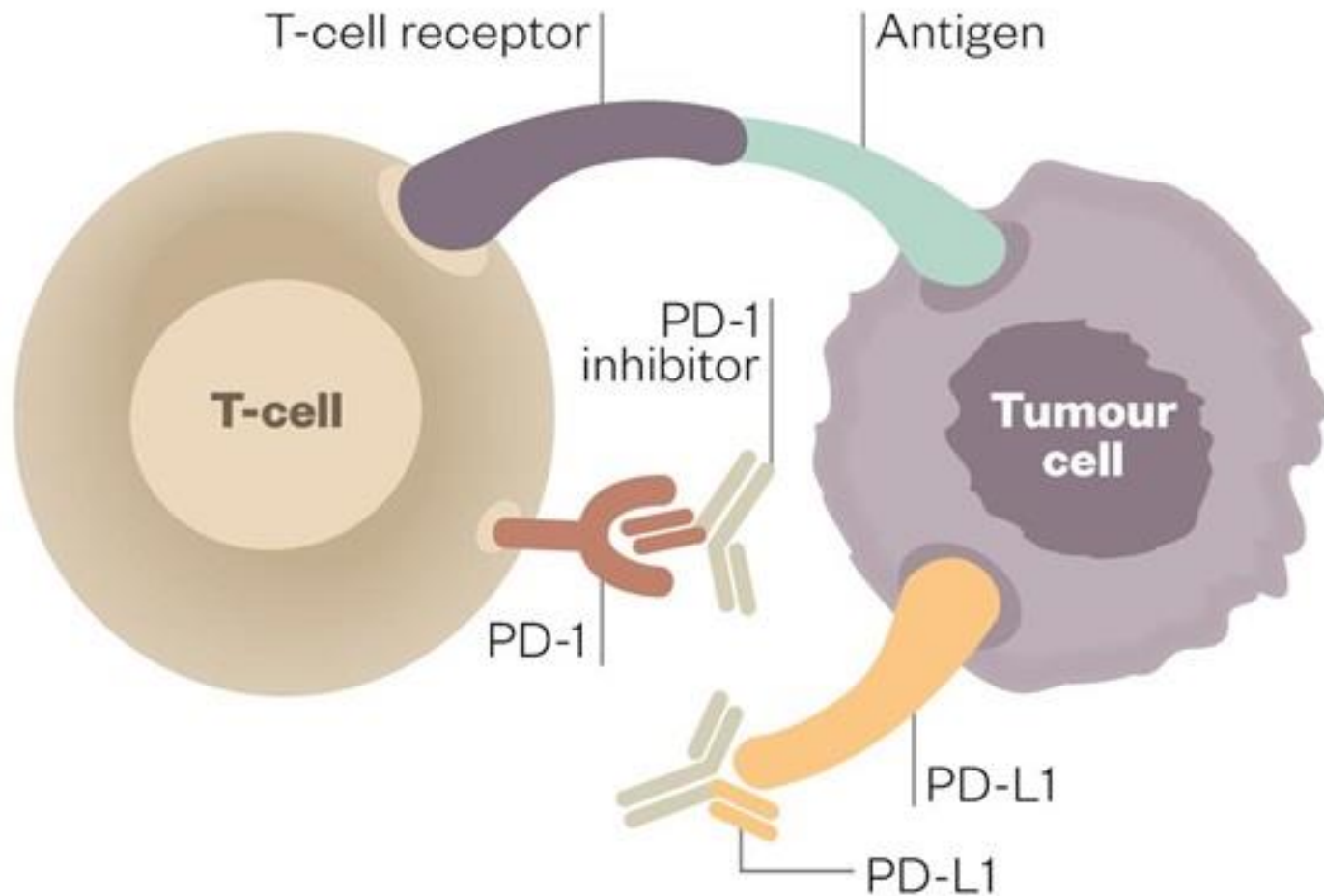


National cooperative group study
National Quality of Life Co-Chair: Dr. Yom, UCSF

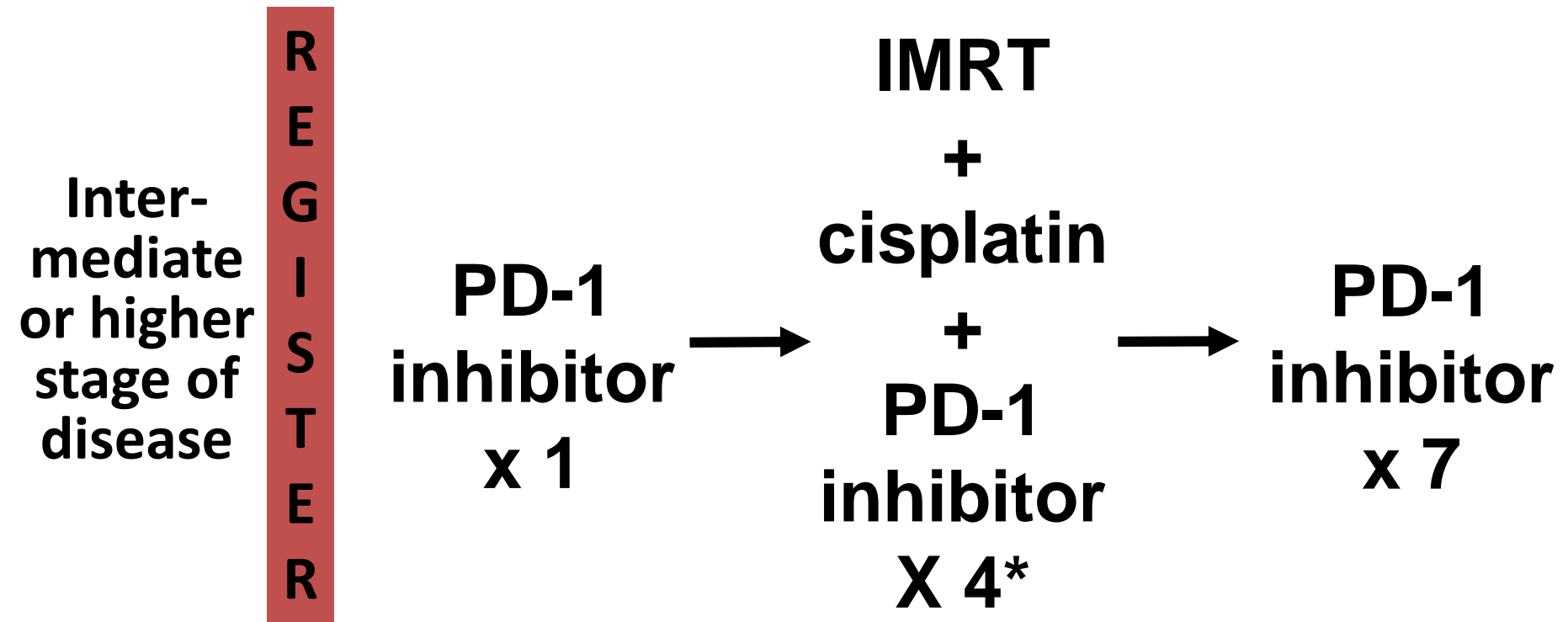
T Cell sees the Cancer Cell - But interaction of PD-1 and PD-L1 deactivates the T Cell



T Cell sees the Cancer Cell - Blocking PD-1/PD-L1 interaction allows the T Cell to activate



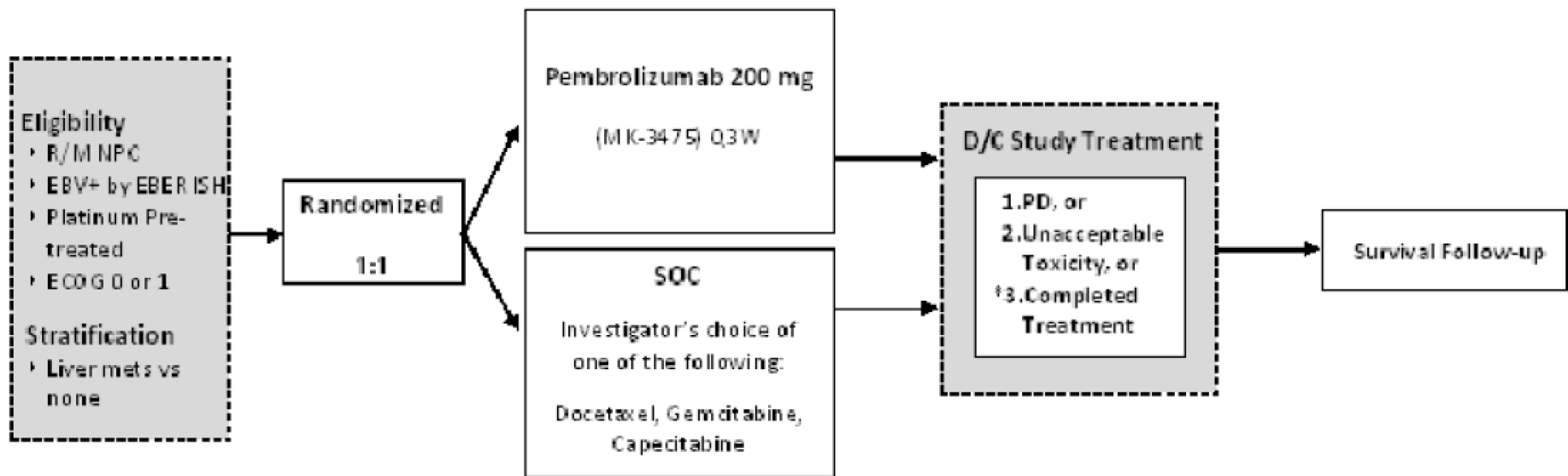
UCSF-Singapore PD-1 Inhibition Study for Newly Diagnosed NPC



Principal Investigator: Dr. Yom, UCSF
Collaborators: NCC and NUH Singapore

* Patients will be tested for EBV, T cells, immunologic markers

Randomized Phase II Study of Pembrolizumab vs Chemotherapy for Metastatic NPC



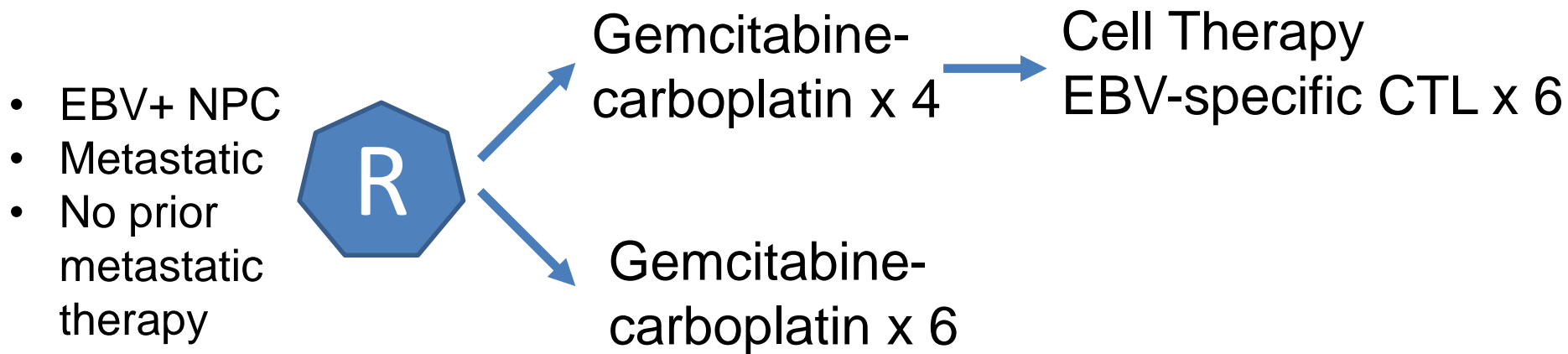
† Second Course of Pembrolizumab

Subjects randomized to Pembrolizumab who completed 2 years of treatment with confirmed response, may be eligible for retreatment with up to 1 additional year of Pembrolizumab at the time of recurrence in Survival Follow-up

Multi-center international study
Site PI: Dr. Algazi, UCSF

Adoptive T Cell Phase III Study for Metastatic NPC

Phase III Clinical Trial of Gemcitabine and Carboplatin followed by Epstein-Barr Virus-specific Autologous Cytotoxic T Lymphocytes vs Gemcitabine and Carboplatin



Multi-center international study
Site PI: Dr. Algazi, UCSF

We welcome any collaborations to advance research in NPC at UCSF

