

How to submit a tissue specimen

- Types of biopsies
 - Incisional biopsy: choose the most representative area to ensure most accurate diagnosis
 - Excisional biopsy: remove the entire lesion to prevent progression or transformation
- Aids in selecting a biopsy site
 - White light exam (Gold standard for recognizing abnormal tissue)
 - Look for ulceration, erosion, vesicles, bulla, macule, papule, plaque, or nodule
 - Note any abnormal textures (granular, verrucous, papillary)
 - Note any abnormal colour (white, red, red+white)
 - Abnormal size or growth
 - Palpation
 - Indurated tissues (fibrotic, firmer) indicated involvement of submucosal tissues
 - Doughy texture suggests a soft tissue lesion
 - Fluctuance suggests an abscess or cystic lesion
 - Blanching, pulsation, thrill, or bruit suggests a vascular lesion (refer)
 - Dental
 - Percussion, probing, vitality testing, and radiographic imaging
 - Necessary if lesion is associated with dentition or gnathic bones
 - Toluidine blue staining
 - Basic dye that binds to acidic molecules (like DNA) in tissue. Dysplastic cells → ↑ DNA → ↑ stain
 - Requires experience to interpret findings properly
 - Fluorescence visualisation with autofluorescence device
 - Excitation with light causes normal mucosa to auto fluoresce
 - Abnormal mucosa loses ability to auto fluoresce
- Other considerations in selecting a site
 - If the lesion is ulcerated
 - Never biopsy in the center (will likely be non specific and non diagnostic)
 - Sample the edge and adjacent the non ulcerated tissue
 - If the DDx includes a vesiculo-bullous/vesiculo-ulcerative lesion (lichen planus, pemphigus, pemphigoid, chronic ulcerative stomatitis, etc)
 - 2 biopsies are necessary
 - 1 from lesional tissue (unless ulcerated) preserved in formalin → used to H&E stain
 - 1 from uninvolved tissue preserved in Michel's/Zeus solution → used for direct immunofluorescence
- Transporting the biopsy to the lab
 - Tissue fixative – 10% neutral buffered Formalin
 - Used for H&E diagnostics
 - Crosslinks amino groups which denatures antigenic targets but preserves the tissue
 - Inhibits proteolytic enzymes and most microorganisms, stabilizing its architecture
 - Tissue preservative – ammonium sulfate and magnesium sulfate solution (Michel's/Zeus solution)
 - Used for direct immunofluorescence diagnostics
 - Precipitates macromolecules, but preserved antigenic targets
 - Inhibits proteolytic enzymes and some microorganisms, and does not stabilize architecture
 - **The volume of fixative/preservative should be 20x the volume of the tissue sample**
- Cell imaging techniques in the lab
 - Hematoxylin and Eosin stain
 - **Hematoxylin**: binds to basophilic/negatively charged substances like DNA and RNA
 - **Eosin**: binds to acidophilic/positively charged substances like proteins, muscle, collagen
 - Samples need to be embedded in paraffin wax prior to staining
 - Direct immunofluorescence
 - Used for diagnosing vesiculobullous lesions and vasculitides
 - Antibody linked to a fluorophore. Antibody binds to IgG, IgA, IgM, complement, fibrin, etc
 - Depending on how much of the antigen there is, they will fluoresce accordingly bright
 - Samples need to be kept in cryoprotective embedding medium

- Submitting the form
 - Patient identifiers must match those on the sample. Sample must contain at least 2 identifiers
 - Radiographs and pictures should be submitted for every case
 - Ideally emailed or submitted online. Not printed
 - Include all details asked on the form
 - Form can be filled online
- How a tissue sample is processed
 - Sample is cut into 3mm pieces, or simply bisected if sample is small enough
 - Tissue is embedded in paraffin wax and cooled to form a block
 - 5um slices are cut by a microtome, placed on a slide, and stained
 - Hard tissue samples like teeth or bone need to be softened in acid first (decalcification)
- When can the patient get their results?
 - Using Canada Post → 3 weeks follow up
 - Using courier → 2 weeks follow up
 - Rushed with verbal report from Pathology Department → 1 week
 - If malignancy is diagnosed, clinician is contacted immediately
 - If decalcification or special stains (fungal, bacterial, immunohistochemistry, in situ hybridization, or immunofluorescence) are needed, then delay by 2~7 days

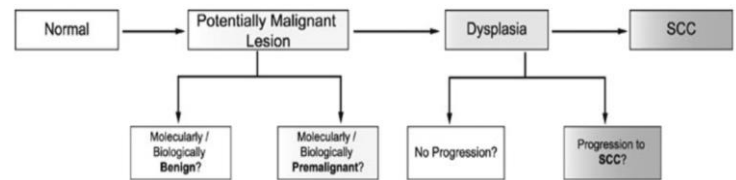
Oral cancer, the big “C”

- Cancer facts
 - 7.4 million deaths per year worldwide
 - 1 in 4 people will die from some form of cancer in the United States
 - Mortality from cancer was greatest in 1991, but has been declining since
 - Head and neck cancer has increased 24.9%, tongue cancer 38.5%, and pharyngeal cancer 50.4% in 2004~2008
- Nutritional issues with cancer
 - Anorexia due to xerostomia, dysphagia, mucositis, fatigue, and maintaining nutrition
 - Cachexia due to tumour tissue that upregulates inflammatory cytokines and causes body wasting
 - Patients look skinny due to loss of lean muscle, fat content remains unchanged
 - Loss of lean muscle also leads to fatigue
- Challenges for patients
 - During diagnosis
 - Time stands still, death denial interrupted, coping or crashing
 - Patients are asked to make very important decisions in a short amount of time
 - During treatment
 - Loss of familiar routines and roles
 - Changes in relationships
 - Financial and practical concerns
 - Fears about treatment and side effects
 - After treatment
 - Transitioning to survivorship
 - Fears of recurrence
- Prognosis for cancer
 - 5 year survivorship →
 - 42% or oral cancers detected in late stage
 - Stage 1 has 80% survival
 - Stage 3/4 has 20% survival
- HPV and oral cancer
 - Virus that causes cervical cancer in women is also linked to cancers in men
 - More than half of oral cancers in men are associated with HPV
 - HPV positive tumors have better response to chemo and radiotherapy, with a 2 year survival of 95%
 - In comparison, the 2 year survival of non HPV tumors is 62%
 - HPV vaccine (Gardasil) covers HPV 16 (subtype seen in almost all cases) – looking for coverage for boys

Cancer Type	1975-1977	1984-1986	1996-2004
All Cancers	50%	54%	66%
Prostate	69%	76%	99%
Thyroid	93%	94%	97%
Breast	75%	79%	89%
Hodgkins Disease	74%	79%	86%
Larynx	67%	66%	64%
Oral	53%	55%	60%
Colon	52%	59%	65%
Non-Hodgkins lymphoma	48%	53%	65%
Leukemia	35%	42%	51%
Multiple myeloma	26%	29%	35%
lung	13%	13%	16%

- Nature of oral cancers

- 91% are squamous cell carcinomas
- Does not follow a linear progression
- Potentially malignant lesions may be benign
- Dysplastic lesions may regress (majority) or progress to SCC









- BC Cancer agency

- Cancer treatment will be the same anywhere in BC, regardless of location
- Every Monday at 11am, a pathologist, surgeon, oncologist, etc review H&N cancer cases that have come in
 - Case is presented and a treatment plan is agreed upon

- Dentist's role in patients with cancer

- Pre-treatment
 - Extract hopeless teeth
 - Eliminate possible sources of oral infection and stabilize the dentition
 - Fluoride trays for xerostomic patients and rinses for mucositis management
 - Instructions on home care
- During treatment
 - Manage oral side effects of cancer therapy
 - If treatment is necessary, contact physician. Do procedure right before next round of chemo and check CBC prior to operation
- Post treatment
 - Manage long term side effects: osteoradionecrosis, graft vs host disease, trismus, poor tissue healing
 - Dental breakdown due to dry mouth and flora becoming more acidogenic
 - Possible hypersensitivity due to radiation damage to pulp
 - Prosthodontics due to surgical defects
 - Triaging patient back into community

- Examples of facial reconstruction (prosthodontics + anaplastology)

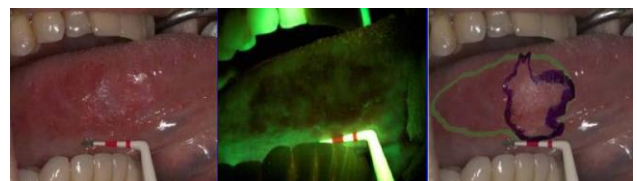
Pre reconstruction	Prosthesis	Final result
		
		

- Positive emission tomography (PET) – newest imaging modality

- Nuclear scan using radioactively labelled tracer molecule with emit positrons as the tracer molecule breaks down
 - 18F-FDG (glucose) most commonly used, based on principle that cancer cells use more glucose than normal cells. Therefore, they light up on PET scans
 - Takes ~2.5 hours and creates a dynamic image of internal tissues and organs
- Areas of inflammation and infection may create false positives
- False negatives possible in younger patients (brain, muscle, etc) or slow growing tumors
- Particularly useful in H&N area, as it has 94~100% sensitivity vs CT with 77~91%
- Not as useful in other cancers like bladder, prostate, cervical, melanoma, etc

- Surgical management of oral cancer

- Cancer needs to be removed and also a margin of normal tissue around it to prevent recurrence
- Fluorescence visualization can aid in outlining a border for cancer removal. Study showed that this method reduced the rates of recurrence
- Done by ENT surgeons. Simple T1 cases can be done by oral surgeons as well



- Radiation therapy of H&N cancer
 - Starts with multidisciplinary consultation and dental assessment
 - Extractions, prophylactic treatments, treatment planning, etc
 - A mould will be formed for the patient to immobilize them
 - Prevents movement during radiation therapy
 - If extractions were planned, mould should be taken many days after to make sure swelling has gone down
 - CT “contouring” will be done to identify exact area to radiate and proper dose will be calculated
 - Methods of radiation delivery
 - **External beam radiotherapy:** treatment from the outside in. Can be done in 2 ways
 - Intensity modulated radiotherapy: using a computer to calculate exactly where to apply radiation to avoid vital structures while killing the tumor. Takes 6~7 hours for computer to calculate
 - Volumetric modulated arc therapy: VMAT is a linear accelerator that rotates around the patient during treatment. Machine continuously reshapes and changes intensity of the radiation beam as it moves around the body. Accurate, shorter treatment, and overall lower radiation dose
 - **Brachytherapy:** treating from the inside out. Radioactive seeds are planted inside the tumor to avoid external radiation to healthy tissues. Usually done in T1 and prostate surgeries
 - Important considerations
 - Patient concerns: what do they want? Do they want a cure or palliative care? Financial concerns? Is the patient motivated? How is their oral hygiene?
 - Consider how much dose will be given to salivary glands and teeth
 - Anatomical factors – osteoradionecrosis happens more in the mandible
 - Side effects (reported by patients of BC cancer agency)
 - 92% dry mouth, 75% taste change, 63% difficulty swallowing, 48% difficulty with dentures, 43% difficulty with chewing, 38% increase in dental decay
- Chemotherapy of H&N cancer
 - In addition to killing cancer cells, chemotherapy also manages micrometastases (systemic disease control)
 - In P16 negative (P16 is the marker for HPV) tumors, 5 year survivability goes from 27.2% to 33.7%
 - **Standard regimen:** high dose cisplatin (100mg/m²) q3weeks x 3 doses
 - Not to be used in patients with renal insufficiency, neuropathy, hearing loss, and cardiac dysfunction
 - **Alternative regimen:** cetuximab if patient has a contraindication to cisplatin. Less toxic but less effective
 - Important considerations
 - Drug concerns: stomatotoxicity, myelosuppressive potential
 - Blood counts at time of appointment (neutrophils and platelets)
 - Does the patient agree to treatment? Do they understand all risks? Do they want a cure or palliative care?
- Important consideration in bone marrow transplant and stem cell transplant patients
 - **Autologous transplant:** patient’s blood is taken prior to chemo and re-introduced during chemo. This maintains a functioning immune system
 - Neupogen (G-CSF) may be given to boost the body to make more white blood cells prior to harvest
 - Don’t probe these patients as it may introduce bacteria into the blood harvest
 - **Allogenic transplant:** blood donated from a different source
 - Patient may be on a Hickman line – controversy regarding need to antibiotic prophylaxis with these patients
 - Blood counts at time of dental work
- Cancer therapy myths: THESE ARE NOT TRUE
 - All chemotherapy lowers immune system so elective dental care is not an option
 - Patients with a central venous line will require antibiotic prophylaxis
 - Chemotherapy and radiotherapy directly cause tooth decay and gum disease and mucositis
 - After cancer therapy is complete, oral hard and soft tissues return to normal and can be treated as such
 - Chemo brain is a weak excuse for forgetting stuff
- Boosting the body’s natural defenses to fight cancer
 - Monoclonal antibodies: triggers immune system, blocks growth signals, or prevents vascular neogenesis in tumors
 - Checkpoint inhibitors (nivolumab and pembrolizumab) bind to specific receptors associated with cancers and causes immune system to kill these cells
 - Vaccinations (in HPV) to prevent infection of possible cancer causing virus
 - Oncolytic virus therapy: genetically modified viruses enter cancer cells and kills them, but not healthy cells



Role of general dentists for the oncology patient

- Dental side effects of cancer therapy
 - Mucositis, xerostomia, dysgeusia, caries, nausea, vomiting
 - Dry skin leading to angular cheilitis or cracked/burning skin
 - Myelosuppression causing increased risk of infection (thrush) and risk of bleeding (even when brushing)
 - Having an infection like febrile neutropenia will mean chemo needs to be temporarily stopped
 - Fatigue causing lack of motivation and poor oral hygiene
 - Osteoradionecrosis is possible in radiation therapy
- Pre-chemotherapy
 - Patient education
 - Possible side effects
 - Inform about BC cancer agency oral oncology center for a resource
 - Patient exam (soft tissues, periodontium, and dentition)
 - Assess current and possible sources of infection → avoids serious complications like febrile neutropenia and can decrease pain/discomfort/trismus during chemo
 - Complete hygiene
 - Let patient know that they can refer to you for support during chemotherapy (supportive schedule)
- During chemotherapy
 - Ask oncologist or MD if their type of chemotherapy is myelosuppressive
 - Avoid elective dental tx
 - If tx is necessary, consider the Nadir period: lowest point of blood counts is 7~14 days after chemo
 - Try to address them after this period so that blood counts will be higher
 - Ideally, see patients right before their next chemo round
 - Hickman line or peripherally inserted central catheter (PICC) line
 - Consider antibiotic prophylaxis if patient has one, but not based on evidence
 - Oral hygiene
 - Increase fluoride exposure (Prevident, fluoride rinse post meals)
 - Check for fungal infections (white or white/red patches, metallic taste), especially under appliances
 - Nystatin cream or rinse can be applied to denture before application to help as well
 - If oral hygiene is poor due to lack of motivation and fatigue, give 0.12% CHX rinse
 - CHX rinse may need to be custom made in aqueous solution (normally made in alcohol, which is irritating)
 - Debridements are controversial. Not sure if beneficial or harmful. Try to avoid
 - Mucositis
 - Ice chips while receiving chemo
 - Room temperature 1L water + 1L baking soda + 1 tsp salt daily mix use as often as desired
 - SLS free toothpaste (SLS irritates open sores) like some children's toothpastes
 - Extra soft toothbrush
 - Dab toothpaste on to teeth if brushing is too painful
 - Avoid hot, spicy, acidic, coarse foods, commercial oral rinses (alcohol), and alcohol
 - Viscous lidocaine rinse before eating or socializing
 - Magic mouthwash (different recipe for most centers)
 - Other considerations
 - Do not make removable prostheses until weight is stable. Weight loss affects denture fit
- After chemotherapy
 - Start with 3~4 month hygiene recalls for 2~3 sessions. When patient stabilizes, go back to 6~9 month recalls
 - Each recall, apply a fluoride varnish for caries and help with xerostomia
 - Wait 3~4 months post chemo to make appliances
 - Salivary flow returns 2~8 weeks post chemo (if radiation therapy was not involved)
 - Mucositis and other symptoms will gradually resolve
- Restorative material considerations
 - Avoid GI due to adhesive
 - RMGIC works well, and amalgam is good too as it's bacteriostatic
 - Silver diamine fluoride → arrests decay effectively, but turns teeth black. Something to consider though

- Pre-radiotherapy
 - Same considerations as chemotherapy
 - In addition, consider pre-radiation extractions to prevent osteoradionecrosis. Decisions are made on a case-by-case basis. Factors to consider are:
 - **Condition of residual dentition.** Consider extraction if patient has advanced caries, periapical infection, periodontal bone loss, furcation involvement
 - **Dental compliance:** patients with poor dental compliance are recommended to have extractions
 - **Arch involved:** mandibular teeth are scrutinized more closely than maxillary teeth, as maxillary teeth may be extracted with minimal risk of osteoradionecrosis
- During radiotherapy
 - Extractions 2 weeks before radiation
 - Avoid elective dental care after week 1
 - Supportive care
 - Oral hygiene
 - Brush frequently using an extra soft toothbrush or Q tip
 - High F toothpaste (Prevident) might be too expensive, so F gel with a toothbrush may be better
 - Oral mouth rinse (same as chemo)
 - Pain control
 - Jaw opening exercises to prevent trismus
 - Lip moisturizer like Burt's Bees (avoid petroleum as it enhances fungus growth)
- Post radiotherapy
 - Short term side effects
 - Skin irritation
 - Dry mouth and changes in taste
 - Sore throat, laryngitis, and problems with swallowing, dehydration, and possible need for a feeding tube
 - Fatigue and pain management problems
 - Long term side effects
 - Dryness may be permanent, depending on amount of saliva glands in the field. May be so severe that the patient cannot sleep
 - Teeth may be vulnerable to decay
 - Long term problems with swallowing → refer back to cancer agency if this is persistent
 - Persistent hoarseness
 - Small risk of low thyroid hormones
 - Carotid stenosis
 - Dental considerations
 - Saliva will be ropery and plaque will be sticky → needs to be scraped with a scaler or explorer
 - 3 month hygiene recall with OH instruction and fluoride varnish
 - Fluoride varnish can be applied as much as you want, but make sure patient spits it out
 - Encourage patient to open/close jaw and swallow frequently to get less scar tissue
 - Dry mouth aids: xylimelts, xylitol mints, oral sprays, gels
 - Xylimelts have a white side and brown side. Brown side adheres to mucosa. Put it on the non-radiated side to get stimulated saliva release long term
 - Dental care is important to prevent needing extractions which may lead to osteonecrosis. No jaw surgery, implants, or extractions unless fields checked. Refer to oral surgeon or BCCA
 - Oral mucosa
 - Area exposed to radiation will appear pale
 - Red vessels will appear around the radiated site
- Cancer care team
 - Oncologists: medical (specializes in drugs), radiation (specializes in radiation), and surgical (specializes in surgery)
 - Plastic surgeon for reconstruction
 - Maxillofacial prosthodontist
 - Otolaryngologist
 - Oncologic dentist or oral oncologist
 - Physical therapist, dietician, counsellor, etc

Prosthetic reconstruction and surgery

- Patient complaints of prosthetic reconstruction
 - Functional impairment: speech, mastication, swallowing, leakage of saliva, food bolus, and liquids
 - Cosmetic deformity
 - Malocclusion and altered jaw movements
- Challenges of rehabilitation
 - Impaired muscles and nerves leading to difficulty in mastication, speech, swallowing, and oral comfort
 - Hard to control removable prostheses, or even mastication involving a fixed crown
 - Anatomical changes due to tumor resection and reconstruction
 - Xerostomia making mucosa more prone to injury and teeth to caries
- Surgeries that can be done to enhance prosthodontic prognosis
 - **Removal of compromised teeth and tori prior to cancer therapy**
 - Remove teeth that are in the field of radiation, 2~3 furcation involvement, decayed/non-restorable, endodontic lesions, or severely mobile
 - Wait 2 weeks after extractions to start radiation oncology
 - Retention of key teeth
 - **Preservation of the hard palate and removal of soft palate + nasal turbinates**
 - As much of the hard palate should be saved as possible as it supports the prosthesis after tumor removal
 - Soft palate's mobility makes it difficult to form a seal with the prosthesis
 - Nasal turbinates hang low and can swell with allergies. This can impinge on the prosthesis' fit
 - **Skin graft**
 - Skin may be better than oral/nasal mucosa because it is more resistant to abrasion, better denture bearing surface, increased retention/stability, better seal, forms a scar band, limits scar contraction, and increases flexibility of cheek/lip
 - Scar band forms at the junction of keratinized skin and oral mucosa. This band is important due to its elasticity. A prosthesis with an hourglass shape or concavity can be inserted into these sites and the elasticity will give good retention
 - **Manage access to the defect**
 - Traditionally, defects were closed up with free flaps after tumor was removed. Now, it may not be done due to risk of cancer recurrence and needing reaccess
 - However, close the defect if:
 - The patient is debilitated/mentally challenged and can't take care of a prosthesis
 - Patient will get a fibula graft to get hard structure to support the prosthesis
 - **Implants**
 - Improves denture retention, stability, function, esthetics, decreases load on vulnerable mucosa
 - Overall increase in quality of life
 - Success rate in irradiated patients is only 64%. In comparison, it is 95% in healthy and 83% in non irradiated cancer patients
 - Implant coverage
 - Subsidized for cancer patients treated at BCCA if implants are placed 2 years after remission
 - \$500 per implant up to a maximum of \$2000 per arch (compared to \$2200 in private practice)
 - Hyperbaric oxygen may be supplemented with implant surgery
 - 20 daily treatment cycles before surgery, then 10 after (6 weeks at VGH in total)
 - Patient is put in a vessel with high PO₂ → stimulates new blood vessel formation
 - Check with oncologist prior to Tx since if they have recurrent cancer, HBO will feed it more
 - Types of implant procedures
 - Auricular implants: If the patient is missing an ear, two implants into the external acoustic meatus can support a prosthetic ear. Cast bar with clips is favoured for retention and stability
 - Nasal implants: if the patient is missing a nose, two implants can be placed on the floor of the nose, 8~10 mm part. Can also be placed in the glabella, but with a lower success rate
 - Orbital implants: if patient is missing an eye, 3 implants should ideally be placed. However, ~5 implants are better due to high failure rate. Placed on lateral supraorbital rim, lateral rim, and malar body

- Prosthodontic reconstruction

	Immediate	Delayed
Advantages	<ul style="list-style-type: none"> -Good morale -Earlier return to function and society 	<ul style="list-style-type: none"> -Consolidation of healing -Less risk of undetected recurrence and infection -Leisurely planning of reconstruction -Shorter initial surgery -Government subsidized
Disadvantages	<ul style="list-style-type: none"> -Risk of infection and undetected recurrence -Conflict with chemotherapy and radiotherapy -Patient must pay 	<ul style="list-style-type: none"> -Cosmetic deformity -Poor function (speech, mastication, deglutition) -Bad morale

- Obturator

- Maxillofacial prosthesis used to close a congenital or acquired tissue opening
- Primarily used on hard palate and/or contiguous alveolar/soft tissue structures
- Functions:** speech, swallowing, mastication, nasal regurgitation, hypernasal speech, articulation. However, does not mean that these issues are resolved completely
 - Because obturators are solid objects, it cannot seal off dynamic mucosal structures
 - All these limitations can be improved by making implant supported obturators
- 3 obturators will be made for the patient: surgical → interim → definitive
- Surgical obturator
 - Given directly after cancer surgery to be worn for 8~10 days
 - Flat, simple, lightweight piece of plastic held in by clasp retention or wired to bone
 - Should not impinge on skin graft or its junction to the mucosa
 - Maintain normal palatal contours
 - Meant as a scaffold for surgical packing, reduce wound contamination, improves speech, shortens hospital stay, and lessens psychological impact
- Interim obturator
 - Given after patient has healed from surgical resection to replace the surgical obturator
 - Allows for tissue changes and improves function over the surgical obturator
 - Needs to be lightweight as it's only retained by the scar band → can be hollowed out
- Definitive obturator
 - Prosthesis made when further tissue changes or recurrence of tumor are unlikely
- Limitations of obturators
 - Lack of nasal seal causing hypernasality

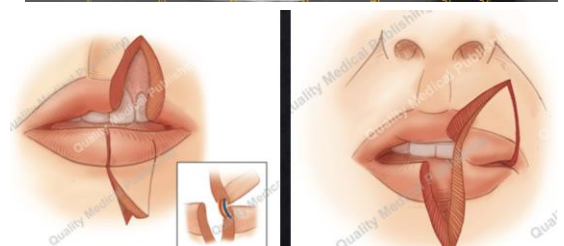
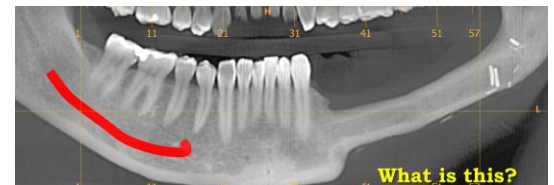


- Future of prosthodontics in these patients


- Currently, patients battling many side effects from cancer treatment cannot be operated on very much due to poor bone healing from radiation therapy
- In the future, implants may be placed at the time of resection surgery
 - Advantages: ↑ osseointegration before radiotherapy, earlier prosthetic rehab, no need for later surgery, no need for HBO
 - Disadvantages: improper placement due to gross anatomic alteration, impairment of prosthodontic treatment, risk delay starting oncologic therapy, possible post treatment complications, and implants may be useless if there is recurrence

- Difference between a flap and a graft

- Flap:** tissue that's resected receives a blood supply
 - Fibula free graft: fibula is taken from leg and planted to missing part of mandible
 - Lip flap: 1/3 of bottom lip or 1/2 of top lip can be cut away and it will heal. This inversion technique is used in patients missing a large portion of the upper or lower lip. Note that there is still connection → blood supply exists
- Graft:** tissue does not have a dedicated blood supply

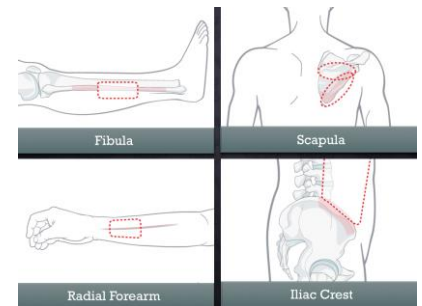


- Overview of prosthetic rehabilitation methods (Dr. Yang's lecture)

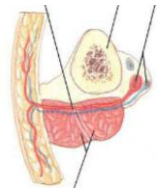


	Background	Lack of nasal seal -Hypernasality -Regurgitation -Food impaction	Unstable dentition -Difficult mastication	Prosthesis mobility -Denture sores -Tissue remodelling
Obturator	-Least invasive option	-Present	-Present	-Present
Implant obturator	-Obturator that's supported by implants	-Improved over obturator	-Improved over obturator	-Improved over obturator
Myo-cutaneous free flap	-Skin used as a flap to seal off area of surgery 	-Resolved	-Present	-No vestibule = no prosthesis retention -Lack of suction on upper prosthesis
Osteo-cutaneous free flap	-Skin and bone harvested -Replaces some missing bone, but not complete recovery of function	-Resolved	-Present	-No vestibule = no prosthesis retention -Lack of suction on upper prosthesis

- Principles of free flaps

- Bone can be taken from the fibula, inferior scapula, spine of scapula, radius, iliac crest
- Tissues in a free flap
 - **Necessary:** artery, vein, and muscle (muscle gives vital vascular bulk, not for contraction purposes)
 - **Optional:** skin, bone, nerve
- Contraindications
 - Any type of peripheral vascular disease (smoking, diabetes, atherosclerosis, collagen vascular disease) because good vessel health is essential for success
 - Coagulopathies or hypercoagulable state
 - Age



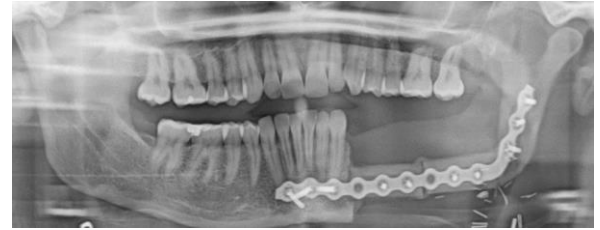
- Each type of bone flap in detail

Flap	Blood supply	Bone	Skin paddle	Pedicle length	Other pros	Other cons
Fibula 	-Peroneal artery -Peroneal vein	-Good -Long strong bone -Bone can be manipulated and will stay vital due to good periosteal blood supply	-Fair (bulky)	-Fairly short	-Sensate (if you get nerve, can regain some sensation) -Simultaneous harvest -Low donor site morbidity (decreased ankle strength and toe flexion)	-Peripheral vascular disease common
Radial forearm 	-Radial artery -Vena concomitant, cephalic vein	-Poor -40% of the radius (in cross section) can be taken	-Good (pliable and mobile), but has cons (thin) -Minimal hair	-Long → good because it can be difficult to find a vessel in the mouth, so this can reach to the neck	-Consistent caliber of artery (rarely affected by PVD) -Tolerates radiation well -Can be sensate -Simultaneous harvest	-Too much radius taken = risk of harming hand function -Minimal bone
Iliac crest 	-Deep circumflex iliac artery -Deep circumflex vein	-Good	-Fair (immobile)	-Short	-Simultaneous harvest	-High morbidity (bowel perforation, hernia, gait disturbance) -Bulky tissue
Scapula (less often used in H&N surgery)	-Scapula circumflex artery -Scapula circumflex vein	-Fair	-Best (multiple available)	-Long		-Bone not as good as fibula or iliac -Simultaneous harvest not possible

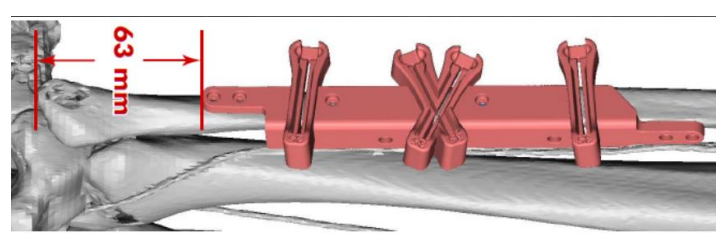
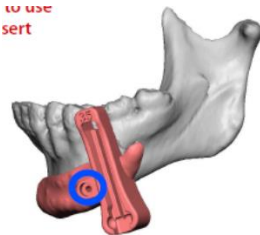
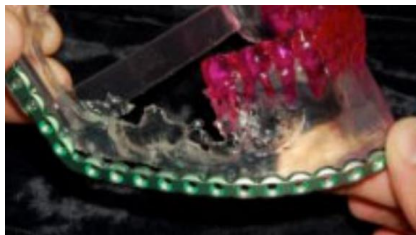
- Workup of reconstruction
 - Prior to surgery
 - Cancer workup: staging, planned resection area
 - Reconstruction: angiogram, assess vessels
 - Post surgery
 - Re-evaluate in 0~6 months to see if post-surgical radiation is needed
 - Wait 2 years before dental reconstruction

- Positioning of the fibula segment

High position	Low position
-Fixation plate screws may damage contralateral teeth	-Best facial contours
-Best dental reconstruction	-Poor dental reconstruction (long crown-root ratio for implant placement)
-Poor facial contours	



- Other considerations: bulkiness of flap impeding airway, position dedicated by soft tissue landmarks, and position dictated by vessel positions



- Surgeries are CT guided
 - Preoperative anatomy is modelled in a computer
 - Metal plate is pre-bent to hold bone fragments in place
 - Mandible cutting guide (middle) and fibula cutting guides (right) can be made, so that cuts are exact length and the fibula will fit into the removed part of the mandible perfectly
 - Gives predictable reconstruction results
- Soft tissue challenges
 - Little to no keratinized tissue on these sites
 - Implants will be coming out of unattached mucosa – lots of movement

Oral complications of treating hematopoietic malignancy

- Blood cancers
 - Bone marrow
 - Myelogenous leukemia (AML, CML)
 - Lymphoblastic leukemia (ALL, CLL)
 - Multiple myeloma (plasma cells)
 - Myelodysplastic syndrome (all cell lines, dysplastic marrow)
 - Aplastic anemia (all cell lines, aplastic marrow)
 - Lymph nodes
 - Lymphomas (B cell, T cell) – Hodgkin's and Non-Hodgkins lymphoma
- Chemotherapy

Induction chemotherapy			Consolidation chemotherapy		
-Primary treatment			-Secondary treatment		
-Induce remission of the cancer			-Kill any residual cancer cells		
-Via central Hickman line			-Via central line		
			-Bone marrow or stem cell transplant possible		
Blood values should be normal when starting:			Blood values should be this in complete remission:		
-Hemoglobin	12.5~17.0	g/dL	-Marrow	<5%	blasts
-WBC	4.0~10.5	e3/dL	-Neutrophil	>1	e3/dL
-Platelet	150~400	e3/dL	-Platelet	>100	e3/dL

- Bone marrow and stem cell transplant
 - Autologous transplant
 - Stem cells in peripheral blood are taken out 1~2 weeks before induction chemotherapy
 - Allogenic transplant
 - Donor stem cells extracted via blood or marrow aspiration (from ilium under GA)
 - Cells are reintroduced into the patient by thawing the sample and giving it via the central line
- Common oral complications
 - Xerostomia and salivary gland dysfunction
 - Submandibular and sublingual glands provide 99% of daytime saliva. These glands are situated close to the mandibular lymph nodes, which receive almost all oral cancers
 - Therefore, the area with these salivary glands are almost always (95%) a target in high dose RT
 - The parotid gland, which provides stimulated salivary flow, is less affected
 - **Dental decay**
 - Chemotherapy/radiotherapy does not affect the enamel, dentin, or cementum directly, but there are indirect changes due to reduced salivation
 - Also, it may cause the oral flora to become more acidogenic
 - Pulp becomes less responsive to infection, trauma, dental procedures, and has some pain/sensitivity
 - Neutral sodium fluoride gel + carrier
 - Tray with fluoride gel applied and worn daily
 - Poor compliance (due to sores) and gives patient false impression that this will halt all caries
 - Tray will do nothing if oral hygiene is not done to clear the plaque
 - May be an option if the patient is highly motivated
 - Other options: toothpaste, remineralizing solutions, diet modification, etc
 - Infections (bacterial, viral, fungal)
 - Candidiasis
 - **Pseudomembranous candidiasis** – white layer that rubs off
 - **Chronic hyperplastic candidiasis** – does not wipe off
 - **Erythematous candidiasis** – redness without the classic white appearance
 - In immunocompromised, candidiasis is not always the same as seen in textbooks
 - **Denture stomatitis** – infection under denture with generalized redness + inflammation
 - Poorly fitting dentures should be avoided in cancer patients
 - **Angular cheilitis** – typically a mixed infection, but could be due to candida
 - Treatment
 - Nystatin oral suspension 10~15 mL rinse and spit/swallow QID x 7~14d
 - Clotrimazole lozenge 10 mg dissolved tid x 7~14d
 - 0.1% Kenacomb ointment for angular cheilitis
 - Oral fluconazole tablets 100 mg po 1d x 7~14d
 - Rinses/lozenges can be used in immunocompetent pts, systemic tx in compromised
 - Herpes viruses
 - Herpes simplex (cold sore)
 - Forms as vesicles along a dermatome and on attached mucosa intra-orally
 - This is a key feature as aphthous ulcers form on non attached mucosa
 - In immunocompromised patients however, HSV can behave differently
 - Anatomical midline not respected and lesions crossing midline
 - Bigger and crustier lesions than a normal cold sore
 - Could lead to huge morbidity, and can be prevented with prophylactic antivirals
 - Varicella zoster virus (chicken pox first time, shingles when reactivated)
 - Can reactivate in immunocompromised or due to sunlight, stress, etc
 - Post herpetic neuralgia after shingles resolution is the biggest long term problem
 - Treated with acyclovir or valacyclovir (Valtrex)
 - Acyclovir is topical and has to be applied 5x/day, so it's not well used
 - Valtrex can be given oral (500mg bid x5-10d) or IV. IV is used in immunocompromised

○ Oral graft vs host disease

Acute Oral GVHD Mucositis



Acute Oral GVHD



Chronic Oral GVHD (lichenoid lesions)



Chronic Oral GVHD (hyperkeratotic plaques)



Chronic Oral GVHD (pseudomembranous ulcerations)



Chronic Oral GVHD (superficial mucocoeles)



Chronic Oral GVHD (candidiasis)



Chronic Oral GVHD (atrophic glossitis)



■ Terms

- **Graft:** tissue taken from a different site without taking the associated blood supply
- **Histocompatibility:** cell surface proteins called MHC or HLA need to be matched between the donor and the recipient before transplant
 - HLA/MHC genetic information is located on chromosome 6 and is highly polymorphic
- **Classic graft rejection:** the recipient's immune system recognizes the donor's graft tissue as foreign, so this triggers an immune reaction against the graft
- **Graft vs host disease:** the recipient's immune system is wiped out (cancer Tx), and when the donor's graft is introduced, the graft attacks the recipient
 - Essentially the opposite of graft rejection. "Graft rejects the host"
 - Can even happen in related siblings or HLA identical donor

■ 3 Billingham criteria for GvHD

- Graft has functioning immune cells (immunocompetent)
- Recipient has antigens that are foreign to the donor (histo-incompatibility)
- Recipient is immunocompromised and unable to inactivate donor immune cells

■ Mechanism

- T cells in the graft see recipient tissues as antigenically foreign → secretes TNFα and IFNγ → immune response against host

■ Fine balance between too much and too little

- Having some GvHD is good because it means there is no transplant rejection by the recipient
- Also, it shows the graft was successful and the grafted tissue didn't die out
- Provides a graft vs tumor effect in immunocompromised patients
- Having too much oral GvHD is bad because it significantly increases risk of oral cancer

■ Risk factors

- **Recipient:** older age, total body irradiation, diagnosed with CML or MDS
- **Donor:** older age, high CD3 T cell in graft
- **Donor-recipient relationship:** unrelated, mismatched HLA, female donor + male recipient

■ Symptoms

- Oral symptoms: oral pain, food sensitivity, trismus, dry mouth, transient mucocoeles
- Chronic GvHD disease mimics: lichen planus, Sjogren's syndrome, scleroderma, SLE, dermatomyositis, and primary biliary cirrhosis

	Acute GvHD	Chronic GvHD
	-First 100 days post transplant	-Persist >100 days post transplant
General Sx	-Erythematous maculopapular rash -Diarrhea -Elevated liver enzymes -Increased risk of chronic GvHD	-Lichen planus-like changes and sclerosis of skin/mucosa -Sicca syndrome in eyes and salivary glands -Liver involvement with cholestasis -↓ lung fxn 2° to bronchiolitis obliterans
Oral Sx	-Oral mucositis -Mucosal erythema and ulceration -Painful desquamation -Mimics chemo-induced mucosal changes	-Lichenoid changes -Ulcerations and mucosal atrophy -Salivary gland dysfunction -Restricted oral opening -Frequently refractory to systemic treatment

■ Diagnosis/staging chronic oral GvHD

- **3 criteria:** lichenoid reactions (usually on buccal mucosa and tongue), hyperkeratotic plaques, restriction of mouth opening from sclerosis
- **4 stages:** 0 = no Sx, 1 = mild Sx not limiting oral intake, 2 = mod Sx partially limiting oral intake, 3 = severe Sx majorly limiting oral intake

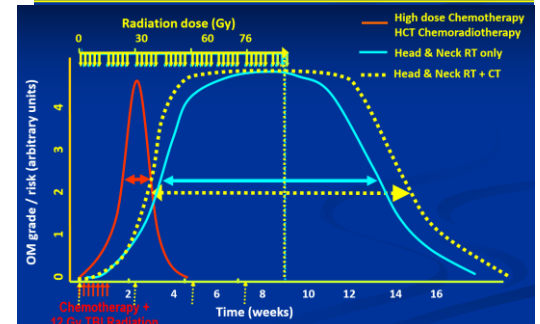
■ Clinical management

- Used to biopsy @ day 100, but current guidelines are to record clinical findings and treat GvHD only if it's symptomatic
 - **What to record:** salivary output, mouth appearance, mouth feeling
- Consider baseline biopsy for areas of persistent change
- Symptoms can be managed with topical steroids. If it does not work, then use systemic steroids
- Lichenoid lesions associated with GvHD have a high risk of oral cancer: 1~2%!

- Oral mucositis

- #1 symptoms reported by patients – “common cold” of cancer treatment. Chart shows % affected →
- Grade 3~4 means very very bad mucositis
- Radiation damages basal layer of mucosa → dead cells at CT-epithelium junction → inflammatory cytokines released → breakdown of epithelium + CT → pain
- Risk factors
 - Previous history of mucositis or genetics
 - <20 or >50 years old
 - Poor oral hygiene, periodontal disease, dentures, xerostomia
- Deciphering the graph on the right
 - Red line: high dose radiation and chemo to kill the immune system. This is done before stem cell transplant. Mucositis kicks in hard, but goes away quickly too
 - Blue line: long RT causes risk of OM to increase as time goes on and healing takes longer too
 - Yellow line: OM kicks in sooner and lasts longer if chemo + radio is used
- Therapy related factors
 - Chemotherapy: dose, regimen, schedule
 - Radiation: dose, fractionation, head and neck proximity
 - Fractionation: giving a big radiation dose over many small doses ↓ risk of mucositis
 - Graft vs host disease prophylaxis
- Management

Cancer Therapy	Any Grade (%)	Grade 3-4 (%)
Head & neck radiation therapy	85 - 100	25-45
Stem cell transplant	75 - 100	25-64
Myelosuppressed pts with solid tumors	5 - 40	5-15
Adjuvant Chemotherapy	10	very rare



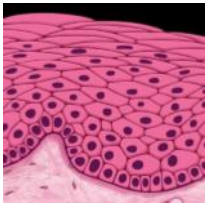
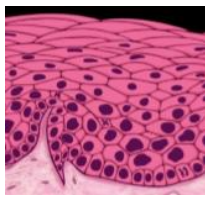
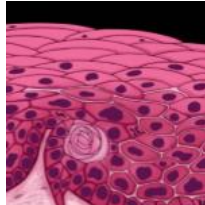
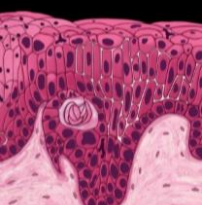
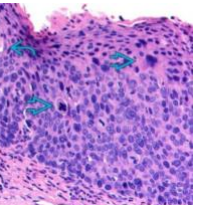
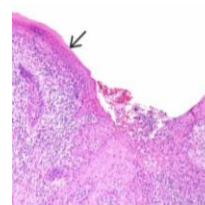
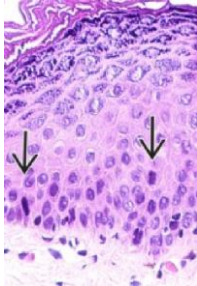






Prior to cancer Tx	Step 1 (foundations of care)	Step 2 (mild pain + dysfxn)	Step 3 (mod pain + dysfxn)	Step 4 (sev pain + dysfxn)
-Complete dental exam -Dental disease stabilization (acute and chronic complications) -Patient education and motivation*	-Preventative measures PRN (palifermin, oral cryotherapy, lasers) -Oral hygiene and flossing* -Frequent multidisciplinary assessments -Bland rinses*	-Topical anesthetics and mucosal protectants* -Mild analgesics (non opioid or mild opioid) -Diet modifications	-Mod strength opioids -Sustained release opioids -Diet/fluid modification	-Strong opioids -Hyper-alimentation (AKA feeding tube)

- “Patient education”
 - Adequate nutritional and fluid intake – consider working with a nutritionist
 - Should be monitored closely for caries, frequency should be determined by caries rate, xerostomia, etc
- “Bland mouth rinse”
 - 1tsp baking soda, 1tsp salt, 4 cups water, mixed daily used tid up to every 1 hour
 - Buffers pH, maintains moisture, removes debris, acts as a lubricant
- “Topical anesthetics and mucosal protectants”
 - Many types of mouthwashes under varying names (Pink Lady, Noll’s solution, Magic mouthwash, etc)
 - Usually a variation of: diphenhydramine, viscous lidocaine, aluminum hydroxide, nystatin, corticosteroid
- “Oral hygiene”

Brushing	-Soft bristled brush within 30 minutes of eating and before bedtime -If bleeding persists >2mins and/or platelets <20, use moist gauze or foam sponge toothettes and resume normal brushing once platelets are normalized
Flossing	-Floss at least 1x/day with waxed floss. If pt didn’t floss before, don’t start during cancer Tx -Discontinue if bleeding persists >2mins and/or platelets <20
Denture care	-Remove dentures before brushing, brush and rinse after meals and at bedtime. Soak in solution overnight -Smooth rough areas before cancer Tx -If dentures are loose or unstable, minimize use until end of cancer Tx -If new dentures are to be made after cancer Tx, wait until tissues heal and weight stabilizes

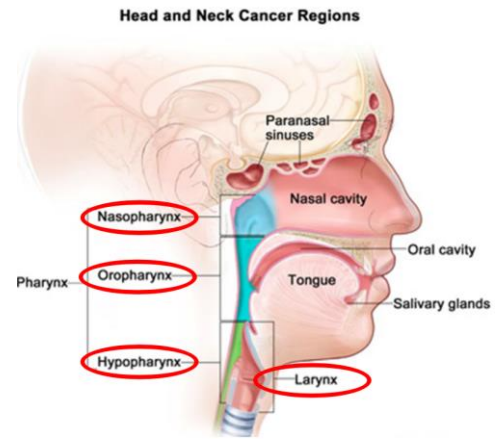
- Dysgeusia
 - Common side effect of oral cancer treatment due to damage of taste cells
 - Less enjoyment of food means high sugar diet is needed to maintain caloric intake
 - Nutritional status impairment, weight loss, less denture retention, denture irritation may arise
 - Psychological dysphagia – trouble swallowing food because it does not taste good
- Dysphagia
 - Persistent dysphagia reported in 50% of H&N chemo/radiotherapy patients
 - Radiation therapy or surgery-induced fibrosis can alter the integrity of the swallowing muscles
 - Tongue range of movement, decreased glottic closure, decreased cricopharyngeal relaxation
 - Risk of aspiration, fear of eating, social isolation, depression
 - Can be worsened by inability to masticate, lubricate, or mobilize food bolus

Dysplasia

Normal tissue	Mild dysplasia	Moderate dysplasia	Severe dysplasia	Carcinoma in situ	Invasive SCC
-Maturation gradient of cells -Smaller or absent nuclei at surface	-Alteration to basal and parabasal layers	-Alteration from basal to mid spinous layer	-Dysplasia of 2/3 of epithelium	-Dysplastic cells in full thickness of epithelium	-Dysplastic penetrating past epithelial layer
					
-Distinctive rete ridges -Epithelium easily discernible from underlying lamina propria	-Larger nuclei to cytoplasm ratio -Nuclear hyperchromasia -Increased mitosis beyond parabasal zone -Possible budding or drop shaped rete  pegs -Hyperchromatic nuclei in basal and parabasal layers -Rest of epithelium matured normally	-Can revert to normal or go to higher grade dysplasia -Atypia through middle 1/3 -Dyskeratosis -Keratin pearl formation -Slightly edematous spacing between cells of hyperchromatic nuclei -Elongated rete -Marked acanthosis -Nuclear pleomorphism -Potentially reversible, but complete removal is warranted if possible	-Keratin pearl formation -Slightly edematous spacing between cells of hyperchromatic nuclei -Elongated rete -Marked acanthosis -Nuclear pleomorphism	-Atypical mitoses -Keratin pearl formation -Intercellular edema -All cells irregular -Pleomorphism -Nuclear hyperchromasia -Pleomorphism -Atypical mitosis  -Dyskeratosis 	   

Head and neck cancer (non thyroid)

- Most common sites
 - Larynx, hypopharynx, oral cavity, and oropharynx
 - 5% of all cancers
 - Larynx used to be the most common H&N cancer, but now it is the oropharynx
 - Squamous cell carcinoma
 - 2015: affects 3.7/100,000 males (been decreasing, likely due to decrease in smoking)
 - Nasopharynx
 - More common in Asia and North Africa
 - 18% of all cancers in South East Asia
 - Undifferentiated, non keratinized carcinoma
 - In the oral cavity?
 - Tongue, buccal mucosa, and gingiva
 - Even though H&N cancer only makes up 5% of all cancers, the workload required to treat them is 5x that of a typical lung or breast cancer. Complicated to make a management plan due to all the side effects



Comparing H&N cancers

	Oral, larynx, oropharynx cancer		Nasopharynx cancers
Risk factors	-Human papilloma virus -Tobacco and alcohol -Ultraviolet sun exposure	-Betel nuts -Saw dust -Asbestos	-Epstein Barr virus -Salted fish, smoked meat -Wood fires, dust, smoke -Genetics
Signs and symptoms	-Most common: lump or mass in the neck that is non-resolving -Pharynx: hoarseness, dysphagia, odynophagia -Otolgia -Mouth: halitosis, sores, non healing ulcer, erythroleukoplakia, loosening of the teeth, ill fitting dentures		-Painless lump in neck -Otolgia -Nasal obstruction -Epistaxis -Hearing loss -Headaches -Diplopia

- Treatment of nasopharynx cancer can depend on cause
 - Smoking related cancer is stubborn and relatively radioresistant (>7 weeks of radiotherapy needed)
 - Virus related cancer "melts away" with radio or chemo
- Similarities between oral, larynx, oropharynx, and nasopharynx cancers
 - Cells are poorly differentiated
 - Often have nodal metastasis, and distant metastasis is not unusual
 - Very sensitive to chemo/radiotherapy with good prognosis
 - Malignant cells in lymph node cause an inflammatory reaction, so will usually cause some tenderness

Diagnosis (done at ENT clinic)

- Fine needle aspiration of lesion/lump biopsy
- Incisional biopsy
- Indirect mirror examination
- Rigid laryngoscopy
- Flexible nasopharyngoscopy
- Examination under anesthesia



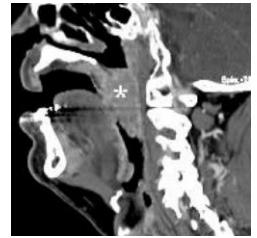
Multi-disciplinary team

- ENT surgeon
- Radiation oncologist
- Medical oncologist
- Oral oncologist (trained dentist)
- Dietician
- Speech pathologist
- Nurses
- Weekly provincial H&N conference

- Staging/imaging

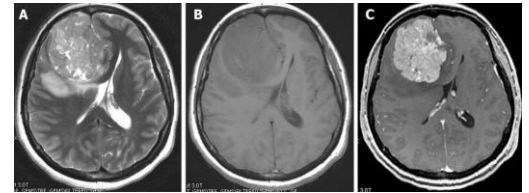
- Computed tomography scans

- Series of X rays are taken and a 3D image is constructed via a computer
 - Scan will show electron densities of tissues: hard tissue (bone) > soft tissue (water filled tissues) > air (lungs)
 - Air filled tissues = very little electron density = all X rays pass through = appears black
 - To see areas of interest, some contrasting dye can be used
 - Dye can be put into the body via ingestion (intra-luminal route) or injection (intra venous)
 - Vascularized tissues will pick up contrast dye well
 - Does not guarantee that tumour will be imaged though
 - Anatomical imaging – good for finding anomalies by comparing L/R sides, but not much more



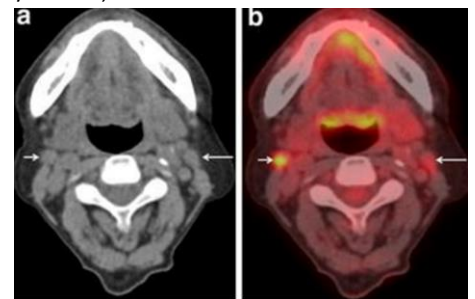
- Magnetic resonance imaging

- Magnetic field is applied to align protons in H₂O
 - Radio waves alter spin of protons and detect their relaxation
 - Gradient is formed solely based on how water acts in different types of tissues
 - Scan will show radiofrequency pulse of various tissues
 - T1 pulse (B): white matter shows as white, gray matter shows as gray, fat shows bright
 - T2 pulse (A): shows water as bright
 - T1 and T2 (C) are combined to show a diagnostic image
 - IV contrast gadolinium can alter relaxation and aid in imaging
 - Anatomical imaging – good for finding anomalies by comparing L/R sides, but not much more



- Positron emission tomography scans

- Functional molecule has a positron attached to it and is injected into the body
 - Common functional molecules used:
 - FDOPA – used to attach to certain brain tumours
 - EF5 – used to attach to hypoxic tissues
 - F18-FDG – sugar molecule used to attach to tumours, inflammatory cells, or infections
 - Positron splits into 2 gamma rays and is detected
 - Produces a fuzzy image, but can be overlaid with a CT scan to get diagnostic image
 - The brain and heart always light up due to high activity, so not as useful for diagnosing cancers here
 - The bladder always lights up due to it being the excretion pathway, so not useful here either



- Treatment

- Small tumours

- Single modality of treatment
 - Usually one of radiation or surgery

- Large tumours

- Combined modality of treatment
 - [Radiation + chemotherapy] or [Surgery +/- radiation +/- chemotherapy]
 - Consider location of tumour too. Delicate areas like soft palate/larynx may be better to do non-surgery

- What kind of surgery?

- **Oral cavity/oropharynx:** partial/total glossectomy, wide excision (FOM, buccal mucosa), laser surgery
 - **Larynx:** partial/total laryngectomy
 - **Neck dissection:** gross lymph node dissection as a prophylactic measure
 - Small resections will have a few permanent side effects, and large resections may cause:
 - Tongue: phonation, dysarthria, mastication, dysphagic problems
 - Jaw/bone: appearance, speech, mastication problems
 - Voice box: phonation, airway protection problems
 - Neck dissection: neck and shoulder mobility problems
 - Keep note that you want 1cm borders around the cancerous tissue when surgically excising it

- History of radiation therapy

Early years	-Radiation used for growths and lesions like lupus, rodent ulcers, and epitheliomas -1915~1935: public health concerns of radiation, as it caused fibrosis, ulceration, and late malignancies -1934: Henri Coutard develops a fractionated regimen to use radiation for treating H&N cancer. Caused a severe but recoverable mucosal reaction, and had a 23% success rate
Intermediate years	-Modernization of brachytherapy -1950~1970: Megavoltage (~1MeV) radiation therapy -1970~1980: 6~18 MeV in iso-centric beams
Knowledge years	-1984: Dr. Vikram had only 13% recurrence rate of H&N cancers when radical neck dissection was added with radiation therapy. This is in contrast to 54~71% recurrence in 1969 -1980~1990: radiation therapy aimed at organ preservation -1992~1999: maybe more radiation isn't always better, because patient may suffer severe SE's and even loss of organ function. Just because an organ was preserved, does not mean it is functional

- Radiotherapy side effects

- Temporary: dry skin, dysphagia, odynophagia, mucositis, pharyngitis, laryngitis, dysgeusia, fatigue
 - Dysgeusia and mucositis may make eating unappealing to patient → possible severe weight loss
 - See dietician so patient meets proper nutrition demands
 - Taste will return to 80~90% of normal, younger the faster. Savory comes back first, then sweetness
- Permanent: xerostomia
 - Serous component is most damaged by radiation
 - Saliva becomes thick → constantly spitting during the day, and lumping during sleep
- Late: fibrosis, hypothyroidism (20~30%)

- Chemotherapy side effects

- Nausea, vomiting, anorexia
- Neuropathy, mouth sores
- Alopecia
- Cytopenia
- Skin rash
- Fatigue
- Dose is delivered to whole body, so more systemic side effects

- Treatment options for chemotherapy

Neoadjuvant

- Cytorreduction (alone)
- Cisplatin + Gemcitabine

Concurrent

- Organ preservation
- Radiation sensitizer
- Locally advanced
- Cisplatin, Cetuximab

Adjuvant

- Post-operative, concurrent with RT
- Locally advanced
- Cisplatin

- Recurrence

Curative treatment available for recurrent disease

- HNFU (Endoscopy)

- 1st Year: q1-3 months
- 2nd Year: q2-4 months
- 3rd to 5th Years: q6-12 months

- Radiology

- NPC: MRI 3 months post RT
- SCC: CT or PET/CT, 3 months post RT

- Most recurrences within 2-3 years

- 2nd primary: 2-4% per year



Psychologic aspects of dental pain

- Complexity of pain
 - Pain is a complex experience: affect, cognition, behaviour, neurobiology
 - Comorbidities (psychiatric illness, cognitive impairment) can complicate diagnosis
 - Strong interaction between emotional state and experience of pain
- Prevalence of chronic pain
 - 30% of population in US
 - >50% in those aged >70
- Pain and depression
 - 60% of depression patients report pain at diagnosis
 - Study showed baseline depression was better predictor of future pain than initial pain ratings
 - Depression is a better predictor of disability than pain intensity and duration
 - Treating depression (antidepressants, psychotherapy) may reduce pain
 - Chronic pain patients
 - 30~50% of patients at chronic pain clinics meet criteria for MDD (major depressive disorder)
 - Chronic pain 4x more common in patients with depression
 - Chronic pain patients have increased rates of suicidal ideation, suicide attempts, and suicide
 - Depression in chronic pain should be treated and not assumed to be “normal”
- Pain and anxiety
 - 30% of patients with chronic pain meet criteria for an anxiety disorder
 - PTSD symptoms stronger predictor than other accident-related variables for chronic pain 1 year after an accident
 - Anxiety about worsening pain or reinjury can negatively affect rehabilitation
- Pain and somatic symptom disorder
 - Patient obsesses over why they have pain → distressing or causes significant disruption of daily life
 - Persistent and excessive thoughts, feelings, or behaviours of pain + one of:
 - Disproportionate and persistent thoughts about seriousness
 - Persistently high anxiety about it
 - Excessive time and energy devoted to it
 - Injured workers with somatic symptom disorder with predominant pain:
 - Have more sites of pain
 - Are more likely to have pain that spreads beyond area of original injury
 - Use greater amounts of benzodiazepines and opiates
 - Show greater involvement in litigation
 - This is not malingering or “made up” → neuroimaging shows differences in several brain areas
 - Overall, fairly rare in chronic pain
- Chronic pain and substance abuse
 - Prevalence between 3 and 19%
 - US uses 80% of world’s opioids despite being only 5% of world population
 - Easy to mistake anxiety about having adequate medication supply for addiction
 - Patients with substance use disorders are at increased risk for chronic pain
 - Risk of stigmatization and undertreatment
- Psychiatric medications for neuropathic pain
 - Tricyclic antidepressants (nortriptyline)
 - Duloxetine (SNRI)
 - Gabapentin and pregabalin
- Psychotherapy for chronic pain
 - If someone believes pain, depression, and disability are inevitable → beliefs are likely to contribute to increased pain and disability
 - Cognitive Behavioral Therapy can be used to test and alter beliefs
 - Sense of self-efficacy or control can improve pain experience

- Risk factors and barriers in mental illness
 - Poor diet, smoking and other substance abuse
 - Medication side-effects (e.g. dry mouth)
 - Poor oral hygiene
 - Lack of income and dental insurance
 - Mistrust of dental health professionals, not knowing how to seek help, no phone, lack of insight
- Cognitive distortions in dental patients
 - Catastrophization, magnification
 - Emotional reasoning
 - Black and white thinking regarding helplessness
 - Rumination and avoidance → negative cycle
- Psychological profile and dental pain
 - Prevalence of problematic dental anxiety between 3% and 20%
 - Anxious patients may require more time for breaks and extra explanations
 - Study: in 62 patients undergoing wisdom teeth exos under general anesthesia, postoperative pain was slower to resolve in patients with pre-morbid psychological distress
- Dealing with patients with dental fear
 - Ask the patient about anxiety
 - Use a screening tool such as the GAD-7, Modified Dental Anxiety Scale, Dental Fear Survey
 - Help the patient direct attention away from the pain
 - Maintain open communication about symptoms and possible adverse effects
 - Refer to Psychiatry, Psychology, Social Work, Counsel
- How a referral to psychiatry may help
 - Psychiatric medications can be effective in treating pain (e.g. gabapentin and nortriptyline for neuropathic pain)
 - Reducing anxiety, depression, and/or insomnia can reduce need for analgesics
 - Can help assess contribution of any substance use disorder
 - Referral to Psychiatry should be done in a thoughtful way
 - “We can’t find anything wrong with you, so it’s probably psychological” won’t help your patient
 - Explaining that the experience of pain is complex and that different specialists can make different contributions to reducing their discomfort
 - Earlier involvement is better

Psychologic aspects of dental pain in an oncologic setting

- Survivorship of cancer treatment
 - Patients cope really well until they go into remission → enters the “Vacuum effect”
 - Loss of “active” treatment, loss of contact with doctors and nurses
 - Uncertainty, fear of recurrence
 - Hard to go back to normal life: relationships, work
 - Regular life has continued on without them
 - Some family and friends may not have been supportive
- Anxiety in cancer patients
 - Prevalence of 7 – 44% , with “adjustment disorder with anxiety” being the most common diagnosis
 - No consistent evidence to show site or stage of cancer affecting prevalence
 - Depression often accompanied by panic symptoms
 - Long hospitalizations / ICU may cause PTSD
 - May manifest as insomnia - “Are you afraid to close your eyes at night because you feel you may not wake up?”
 - Etiologies to rule out:
 - Pain, hypoxia, delirium, sepsis, bleeding, PE, hypocalcemia, substance use, medication use
 - Medications: steroids, antiemetics, bronchodilators, hormonal agents
 - Treatment
 - Correct reversible medical etiologies
 - Psychotherapy (CBT, supportive, psychoeducation, validate emotions, mood logs to find triggers)
 - Medication (but check for CYP450 interactions, lorazepam good for nausea)

- Depression in cancer patients
 - Prevalence in cancer ranges from 3 – 58% depending on the exact population/setting
 - Estimated to be 4X more prevalent than in general population
 - Pancreatic cancer (depression related to inflammation/immune/cytokine models of depression)
 - IL6, a marker for inflammation, is found to be higher in patients with depression
 - Cancer patients have elevated IL6, meaning it may be the cause for depression
 - Head and Neck cancer (link to depression thought to be substance use associated with premorbid mood disorder)
 - Diagnosis
 - Neuro vegetative symptoms likely to be present with or without depression
 - Inclusive approach: count things like fatigue and appetite in number of symptoms
 - Etiologic approach: count them only if convinced due to depression
 - Exclusive approach: low energy, poor appetite, etc. don't count
 - Substitutive approach:
 - Drop: appetite or weight change, fatigue, psychomotor disturbance, and impaired concentration
 - Add: irritability, tearfulness, social withdrawal, and feeling punished
 - Increased threshold approach: all symptoms listed in DSM count, but need more than 5
 - Ask the money questions: hopeless, worthless, guilty, feeling like being punished, suicidal ideation
 - Just ask them: "Have you been depressed most of the time for the past two weeks?"
 - 100% sensitivity, 100% specificity in 197 patients with advanced cancer in a palliative care setting
 - Better than Beck Depression Inventory in the same study
 - Psychopharmacology
 - Fluoxetine and desipramine both effective in reducing depression and improving quality of life in depressed women with advanced cancer
 - Psychotherapy
 - Cognitive behavioural therapy (CBT)
 - Others: Meaning Centered Psychotherapy, Dignity Therapy, Managing Cancer and Living Meaningfully
- Suicide in cancer patients
 - 2-3X increased risk for suicide compared to general population (1-16% prevalence of suicidal ideation)
 - Risk factors
 - Depression, hopelessness, loss of control, isolation
 - Personal and family history
 - Pain, fatigue, delirium, advanced illness, poor prognosis
 - Premorbid psychiatric illness/addiction
- Total pain
 - Physical, spiritual, psychological, and social suffering
 - Related to existential suffering
- Existential suffering in cancer patients
 - What is it?
 - Lack of meaning or purpose, loss of connectedness to others, difficulty finding sense of self
 - Thoughts about the dying process, loss of hope, struggle around the state of being
 - Challenges of freedom and choice, spiritual distress
 - Associated with
 - Reduced quality of life
 - Increased anxiety, depression, and suicidal ideation (desire for hastened death)
 - Relationships likely bi-directional and these are modifiable variables
 - Addressing Existential Suffering
 - In terminally ill pts, the strongest predictors of desire for hastened death are depression and hopelessness
 - Stronger predictors than poor physical function
 - These are variables we can influence