การเปรียบเทียบผลของการใช้เครื่องมือฝึกอ้าปากแบบพลวัตและแบบอพลวัตต่อระยะอ้าปากใน
ผู้ป่วยโรคมะเร็งบริเวณศีรษะและคอที่ได้รับรังสีรักษา

นางสาวจารุมนต์ ศิรประชา

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต
สาขาวิชาศัลยศาสตร์ช่องปากและแม็กซิลโลเฟเชียล ภาควิชาศัลยศาสตร์
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ปีการศึกษา 2557

COMPARATIVE STUDY ON THE MAXIMUM MOUTH OPENING BETWEEN DYNAMIC AND STATIC JAW EXERCISE IN IRRADIATED HEAD AND NECK CANCER PATIENTS

Miss Jarumon Sirapracha

A Thesis Submitted in Partial Fulfillment of the Requirements
for the Degree of Master of Science Program in Oral and Maxillofacial Surgery
Department of Oral and Maxillofacial Surgery
Faculty of Dentistry
Chulalongkorn University
Academic Year 2014

Thesis Title	COMPARATIVE STUDY ON THE MAXIMUM MOUTH OPENING BETWEEN DYNAMIC AND STATIC JAW EXERCISE IN IRRADIATED HEAD AND NECK CANCER PATIENTS
By	Miss Jarumon Sirapracha
Field of Study	Oral and Maxillofacial Surgery
Thesis Advisor	Associate Professor Somchai Sessirisombat, D.D.S., M.D.

Accepted by the Faculty of Dentistry, Chulalongkorn University in Partial Fulfillment of the Requirements for the Master's Degree

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จารุมนต์ ศิรประชา : การเปรียบเทียบผลของการใช้เครื่องมือฝึกอ้าปากแบบพลวัตและแบบอพลวัตต่อระยะอ้าปากในผู้ป่วยโรคมะเร็งบริเวณศีรษะและคอที่ได้รับรังสีรักษา (COMPARATIVE STUDY ON THE MAXIMUM MOUTH OPENING BETWEEN DYNAMIC AND STATIC JAW EXERCISE IN IRRADIATED HEAD AND NECK CANCER PATIENTS) อ.ที่ปรึกษาวิทยานิพนธ์หลัก: รศ. ทพ. นพ.สมชาย เศรษฐศิริสมบัติร.น., 60 หน้า.

วัตถุประสงค์ของการวิจัย : เพื่อเปรียบเทียบประสิทธิภาพในการบริหารขากรรไกรด้วยวิธีพลวัตและวิธีอพลวัตในการป้องกันการลดลงของระยะอ้าปากในผู้ป่วยโรคมะเร็งบริเวณศีรษะและคอที่ได้รับรังสีรักษา

วิธีวิจัย : วัดระยะอ้าปากของผู้ป่วยโรคมะเร็งบริเวณศีรษะและคอที่ได้รับรังสีรักษาจำนวน 66 ราย โดยบริหารขากรรไกรด้วยวิธีพลวัตจำนวน 20 ราย (นิ้วมือถ่างขากรรไกร) หรือวิธีอพลวัตจำนวน 19 ราย (ไม้กดลิ้นซ้อนกันเป็นตั้ง) ตั้งแต่ก่อนได้รับรังสีรักษา ทุก 2 สัปดาห์ระหว่างการรักษา วันสุดท้ายที่ได้รับรังสีรักษา และ 6 เดือนหลังสิ้นสุดการฉายรังสี โดยใช้ไม้บรรทัดวัดระยะอ้าปากเทอราไบท์ และให้ผู้ป่วยตอบแบบสอบถามเกี่ยวกับความสะดวกในการบริหารขากรรไกรและผลของระยะอ้าปากที่ลดลงที่มีต่อชีวิตประจำวันในการติดตามผลการบริหารขากรรไกรครั้งสุดท้าย นำร้อยละเฉลี่ยของระยะอ้าปากที่เปลี่ยนแปลงไประหว่างก่อนได้รับรังสีรักษากับ 6 เดือน ภายหลังสิ้นสุดการฉายรังสีของทั้ง 2 กลุ่มมาเปรียบเทียบกันโดยใช้สถิติทดสอบทีที่ความเชื่อมั่นร้อยละ 95

ผลการวิจัย : 6 เดือนหลังสิ้นสุดการฉายรังสีรักษาพบว่าระยะอ้าปากของผู้ป่วยในกลุ่มพลวัตและกลุ่มอพลวัตลดลงเฉลี่ยร้อยละ 9.58 ±13.89 และ 4.55 ± 18.84 ตามลำดับเมื่อเปรียบเทียบกับระยะอ้าปากก่อนได้รับรังสีรักษา โดยไม่มีนัยสำคัญทางสถิติ ($p = 0.347$) การบริหารขากรรไกรและระยะอ้าปากที่ลดลงไม่ก่อให้เกิดปัญหาหรือมีผลกระทบต่อชีวิตประจำวัน

สรุปผลวิจัย : ไม่พบความแตกต่างอย่างมีนัยสำคัญทางสถิติของการบริหารขากรรไกรด้วยวิธีพลวัต และอพลวัตที่มีผลต่อระยะอ้าปากในผู้ป่วยโรคมะเร็งบริเวณศีรษะและคอที่ได้รับรังสีรักษา

ภาควิชา ศัลยศาสตร์ ลายมือชื่อนิสิต .....

สาขาวิชา ศัลยศาสตร์ช่องปากและแม็กซิลโลเฟเชียล ลายมือชื่อ อ.ที่ปรึกษาหลัก .....

ปีการศึกษา 2557

5575801632 : MAJOR ORAL AND MAXILLOFACIAL SURGERY
KEYWORDS: STATIC JAW EXERCISE, DYNAMIC JAW EXERCISE, RADIOTHERAPY, 60 DISTANCE

JARUMON SIRAPRACHA: COMPARATIVE STUDY ON THE MAXIMUM MOUTH OPENING BETWEEN DYNAMIC AND STATIC JAW EXERCISE IN IRRADIATED HEAD AND NECK CANCER PATIENTS. ADVISOR: ASSOC. PROF. SOMCHAI SESSIRISOMBAT, D.D.S., M.D., pp.

Objective : To compare the effects on maximum mouth opening distance between dynamic and static jaw exercise in irradiated head and neck cancer patients.

Materials and methods : The maximum mouth opening distance (MMOD) of 66 head and neck cancer patients who received radiotherapy and performed the dynamic (20 patients) and static (19 patients) jaw exercise were measured at pre-radiotherapy , every two weeks during radiation course ,the last day of radiotherapy and 6 months after treatment. The questionnaire on their quality of life and compliance with jaw exercise technique were collected at the last follow-up day. The percentage of MMOD change between pre-treatment and 6 month post-treatment of both groups were compared using independent t-test (a= 0.05).

Result : The average MMOD changes were 9.58% ±13.89% and 4.55% ± 18.84% reduction in dynamic and static group, respectively. Independent t-test revealed no significant difference between both groups (p = 0.347). Both groups were well tolerated with the jaw exercise and the reduction of their MMOD had no effects on their quality of lives.

Conclusion : There was no significant effect on MMOD between dynamic or static jaw exercise technique in patients with radiotherapy of head and neck.

Department: Oral and Maxillofacial Surgery
Student's Signature .....
Advisor's Signature .....
Field of Study: Oral and Maxillofacial Surgery
Academic Year: 2014

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LIST OF ABBREVIATIONS

2D	two dimensions
2DXRT	conventional external beam radiotherapy
3DCRT	3-dimensional conformal radiation therapy
BOT	base of tongue
CMT	chemotherapy
CT	computer tomography
DOMS	delayed onset muscle soreness
EBV	Epstein-Barr virus
ECM	extracellular matrix
GTQ	Gothenburg trismus questionnaire
HADS	hospital anxiety and depression scale
HLA	human leukocyte antigens
HPV	Human papillomavirus
HRQL	health related quality of life
IMRT	intensity-modulated radiation therapy
MID	maximum interincisal distance
MMOD	maximum mouth opening distance
MRI	magnetic resonance imaging
NPC	nasopharyngeal carcinoma
ORN	osteoradionecrosis
PET	positron emission tomography
RT	radiotherapy
SCCA	squamous cell carcinoma
SD	standard deviation
TGF-β	tumor growth factor-beta
UNPC	undifferentiated type of nasopharyngeal carcinoma
WHO	World Health Organization

Chapter 1
Introduction

Background and Rationale

1.1 Head and neck cancer

Head and neck cancer refers to any malignancies arising in the skin of head and neck, nasal cavity, paranasal air sinuses, oral cavity, salivary glands, pharynx, and larynx.(1)

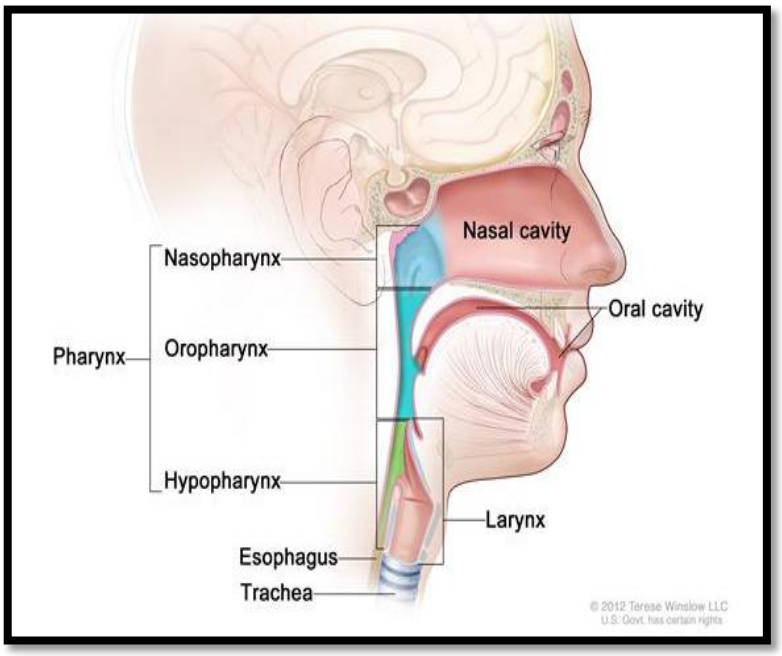


Figure 1 Anatomy of head and neck

Head and neck cancer is the 6th most common malignancy in Thailand. More than 90% of head and neck malignancies are squamous cell carcinoma (SCCA). The most common head and neck cancers in Thailand are the cancers of the lip and oral cavity (49.07 %) followed by nasopharyngeal cancers, other pharyngeal cancers and laryngeal cancers respectively. Nasopharyngeal carcinoma (NPC) is somewhat unique in that squamous cell carcinoma is a minor subtype, with non-keratinizing undifferentiated carcinoma, followed by keratinizing undifferentiated carcinoma being more common.(2) **(Table 1)**

Table 1 Number of head and neck cancers in Thailand 2008 (both sexes) (2)

Sites	Number	Percentage	Rank
Lip, oral cavity	4,398	49.07	1
Nasopharynx	2,058	22.96	2
Other pharynx	1,293	14.43	3
Larynx	1,213	13.54	4
Total	8,962	100	

Etiology

Alcohol and tobacco uses are the most common risk factors for head and neck cancer. Tobacco contains over thirty known carcinogens such as polycyclic aromatic hydrocarbons and nitrosamines etc. whereas the alcohol itself is not a known carcinogen, it may act like a solvent allowing increased cellular permeability of other carcinogens. It is believed that chronic use of alcohol may increase the enzyme cytochrome P-450 which can contribute the activation of procarcinogens to carcinogens. There are several studies supported a synergistic effect of the combined use of tobacco and alcohol on head and neck cancer risk. Smokeless tobacco and in some parts of the world, betel nuts, along with poor oral hygiene are additional risk factors.(3-5) All these factors show dose-response effects.

Ill-fitting denture also associates with oral or oropharyngeal cancer. This may explain the role of chronic inflammation as a risk for oral cancer. Dietary factors may also contribute the diseases. Excessive consumption of processed meat and red meat were associated with increased incidence of cancer of the head and neck, while consumption of raw or cooked vegetables, vitamin C and E, and betacarotene seemed to be protective.(5, 6)

Exposure to some factors also associated with increased risk of head and neck cancer such as wood dust, organic chemicals, coal products, cement, paint, sulfuric or hydrochloric acid and etc. these factors are related with some particular occupations.

Human papillomavirus (HPV), in particular HPV16, is one of the causes for some head and neck carcinoma.(7) Epstein-Barr virus (EBV) is strongly associated with nasopharyngeal cancer.(8)

The head and neck cancer patients often have the familial history of the cancer. This was assumed that there must be association between the genetic factors and the susceptibility of the cancer. Many studies showed relationships between head and neck cancer and p53 tumor suppressor gene. The mutation of p53 tumor suppressor gene may increase the susceptibility to environmental carcinogens. That is why some patients with minimal tobacco exposure develop the head and neck cancer. (5)

Signs and symptoms

The signs and symptoms of the head and neck cancers vary depend on site, severity and involved structures. Presenting signs and symptoms include(5):

- Mass in the neck
- Neck pain
- Bleeding from the tumors
- Sinus congestion, especially with nasopharyngeal carcinoma
- Bad breath
- Sore tongue
- Painless ulcers or sore in the mouth that do not heal.
- Persisted white, red or dark patches in the mouth
- Earache
- Unusual bleeding or numbness in the mouth
- Lumps in the lip, mouth or gums
- Enlarged lymph nodes in the neck
- Slurring of speech (if the cancer is affecting the tongue.)
- Hoarseness of voice or sore throat which persists for more than six weeks.
- Difficulty in swallowing food
- Change in diet or weight loss

Diagnosis

To achieve complete diagnosis and treatment plan, each head and neck cancer patient needs to be evaluated by multidisciplinary team including the head and neck surgeon, maxillofacial surgeons, radiation oncologist, medical oncologist, speech oncologist, nutritionist, social worker, and clinical nurse specialist.

When the patients presented at the hospital with the signs and symptoms of head and neck cancer, the doctor will take a complete history of present illness, medical history, familial history, and the risk factors for cancer. Then the physical examination will be done to achieve overall characteristics of the tumor by inspection and palpation. The endoscope may be used for examining of the head and neck areas. Blood tests may be performed to help diagnose cancer. Testing for viral infections, including HPV, may also be done. The examiner must correlate physical finding with the patient's history. If the cancer is suspected, the biopsy will be operated to make the definite diagnosis. When the head and neck cancer is diagnosed, CT and magnetic resonance imaging (MRI) are useful in the assessment of the deep tissue extension of tumors. Sometimes bone scan and PET scan are helpful for tumor detection of both primary site and metastasis.(9)

TNM staging

TNM staging system is the cancer staging system that describes the extent of a person's cancer. It is based on the extent of the tumor (T), whether cancer cells have spread to nearby (regional) lymph nodes (N), and whether distant (to other parts of the body) metastases (M) has occurred. The objectives of cancer classification include (9):

- To help the physician plan the proper treatment.
- To estimate the prognosis of each patient.
- To evaluate the treatment result.
- To accommodate the communication among the treatment team and personnel involved.
- To assist in the further investigation of the tumors.

TNM staging system of head and neck cancer of the International Union Against Cancer (UICC) 2009. (10)

Primary tumor (T)

Tx primary tumor cannot be assessed

T0 no evidence of primary tumor

Tis carcinoma in situ

- **Lip, oral cavity**

  T1 ≤ 2 cm.

  T2 > 2 – 4 cm.

  T3 > 4 cm.

  T4a lip: through cortical bone, inferior alveolar nerve, floor of mouth, skin

  Oral cavity: through cortical bone, deep/extrinsic muscle of tongue, maxillary sinus, skin

  T4b masticator space, pterygoid plates, skull base, internal carotid artery

- **Nasopharynx**

  T1 tumor confined to nasopharynx

  T2 tumor extends to soft tissues of oropharynx and/or nasal fossa

  T2a without parapharyngeal extension

  T2b with parapharyngeal extension

  T3 tumors involves bony structures of skull base and/or paranasal sinuses

  T4 tumor with intracranial extension and/or involvement of cranial nerves, hypopharynx, orbit, or with extension to the infratemporal fossa/masticator space

- **Oropharynx**

  T1 ≤ 2 cm.

  T2 > 2 – 4 cm.

  T3 > 4 cm.

T4a larynx, deep/extrinsic muscle of tongue, medial pterygoid, hard palate, mandible

T4b lateral pterygoid muscle, pterygoid plates, lateral nasopharynx, skull base, carotid artery

- Salivary glands

  T1 ≤ 2 cm. without extraparenchymal extension

  T2 > 2 – 4 cm. without extraparenchymal extension

  T3 > 4 cm. and/or extraparenchymal extension

  T4a skin, mandible, ear canal, facial nerve

  T4b skull, pterygoid plates, carotid artery

- Nasal cavity and paranasal sinuses

  Maxillary sinus

  T1 mucosa

  T2 bone erosion/destruction, hard palate, middle nasal meatus

  T3 posterior bony wall maxillary sinus, subcutaneous tissues, floor/medial wall of orbit, pterygoid fossa, ethmoid sinus

  T4a anterior orbit, cheek skin, pterygoid plates, infratemporal fossa, cribriform plate, sphenoid/frontal sinus

  T4b orbital apex, dura, brain, middle cranial fossa, cranial nerve other than V_2, nasopharynx, clivus

<u>Regional lymph nodes involvement (N)</u>

Nx regional lymph nodes cannot be assessed

N0 no regional lymph nodes metastases

- N-stage for all sites except nasopharynx

  N1 ipsilateral single ≤ 3 cm.

  N2 a: ipsilateral single > 3 to 6 cm.

  b: ipsilateral multiple ≤ 6 cm.

  c: bilateral/contralateral ≤ 6 cm.

  N3 > 6 cm.

- **N-stage for nasopharynx**

  N1 unilateral metastases in cervical lymph node(s), ≤ 6 cm. in greatest dimension, above the supraclavicular fossa

  N2 bilateral metastases in cervical lymph node(s), ≤ 6 cm. above the supraclavicular fossa

  N3 metastases in lymph node(s)

  - **N3a** greater than 6 cm. in dimension
  - **N3b** extension to the supraclavicular fossa.

Distant metastases (M)

Mx distant metastases cannot be assessed

M0 no distant metastases

M1 distant metastases

Stage grouping

- **Staging for all sites except nasopharynx**

Stage	T	N	M
Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T1, T2	N1	M0
	T3	N0, N1	M0
Stage IVa	T1, T2, T3	N2	M0
	T4a	N0, N1, N2	M0
Stage IVb	Any T	N3	M0
	T4b	Any N	M0
Stage IVc	Any T	Any N	M1

- **Staging for nasopharynx**

Stage	T	N	M
Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage IIa	T2a	N0	M0
Stage IIb	T1	N1	M0
	T2	N1	M0
	T2a	N1	M0
	T2b	N1	M0
Stage III	T1	N2	M0
	T2a	N2	M0
	T2b	N2	M0
	T3	N0	M0
Stage IVa	T4	N0	M0
	T4	N1	M0
	T4	N2	M0
Stage IVb	Any T	N3	M0
Stage IVc	Any T	Any N	M1

Treatment

There are three main alternatives of management of head and neck cancers.

1) Surgery

Surgery is the primary first line of treatment in most types of head and neck cancer. The goal is to remove the cancerous cells completely. Surgery is also commonly used to remove some or all of the cervical lymph nodes to prevent further spread of the disease. But this has to be considered about the disability and deformity after surgery. There are also other several factors to be considered before operation including patient's physical condition, site and invasion of the tumors, type of the tumors, function and esthetic, quality of life, and patient's consent. Surgery maybe collaborated with chemotherapy and radiotherapy.(11)

2) Chemotherapy

Chemotherapy is the treatment of cancer with one or more cytotoxic antineoplastic drugs. Chemotherapy may be given for curative or palliative treatment. It is often used in conjunction with other cancer treatments, such as radiotherapy or surgery. Traditional chemotherapeutic agents act by killing cells which divide rapidly (tumor cells). Meanwhile chemotherapy also destroys rapid divided-cells such as bone marrow cells, digestive tract, and hair follicles. As the results, the most common side-effects of chemotherapy occur including myelosuppression, mucositis, and alopecia. Some newer anticancer drugs (for example, various monoclonal antibodies) are not unspecific cytotoxic, but rather target proteins that are abnormally expressed in cancer cells or essential for their growth. Such treatments are often referred to as "targeted therapy" and are often used together with traditional chemotherapeutic agents in antineoplastic treatment regimens.(5, 12)

I. **Combination chemotherapy**: chemotherapy regimens which consist of many different mechanism drugs to improve tumor cells killing ability.
II. **Adjuvant chemotherapy**: it is given after definitive treatment of the primary tumors to prevent recurrence of the tumors.
III. **Neoadjuvant chemotherapy**: chemotherapy is given before surgery or radiotherapy to reduce the size of primary tumors. It is useful in the case of large tumor that cannot be operated. It helps decrease the complication from surgery or radiotherapy.

3) Radiotherapy

Radiotherapy is the medical use of ionizing radiation to control or kill malignant cells. The principle of radiotherapy is the direct or indirect interaction between proton or electron particles from source of radiation and targeted molecules (DNA chain of malignant cells). Direct reaction occurs when the particles attack the targeted molecules directly. Indirect reaction happens as a result of the ionization of water to form free radicals (hydroxyl) which then damage the DNA. The destroyed DNA will lose its reparative ability and lead to cell death. However the

radiotherapy does not affect only malignant cells but also normal cells, thus the side-effects to surrounding tissues happen as a result.

The effectiveness in malignant cells destruction depend on

1. Radiosensitivity of cells/tumors

   The cells in mitosis phase are more radiosensitive than the resting cells. Therefore labile cells that are highly regenerative such as epithelial cells are more sensitive to radiation than the permanent cells that are incapable of regeneration such as neuron.

2. Oxygenation

   The more oxygen intensity, the more malignant cells are destroyed. Because the free radicals from water ionization integrate with oxygen to form non-restorable organic peroxides in the targeted cell which cause DNA destruction.

3. Tumor size

   The smaller tumor is more sensitive to radiation than the bigger tumor. (13)

Fractionated dose has gradually replaced single dose exposure to improve the therapeutic ratio between normal tissues and tumors. It maximizes the tumor cells death and minimizes damage to normal cells. The principles are explained by 4R's scientific reason.

I. **Repair of sublethal damage**: to let the normal tissue which is slow response to the radiation, to recover from damage.

II. **Redistribution**: in the tumors which have moderate to rapid cell turnover rate, not all cells are in the radiosensitive phase, thus some are not killed in the first radiation. The fractionation allows the residual cells resuming the radiosensitive phase so they may be killed in the next radiation. The redistribution generally gains the therapeutic result.

III. **Regeneration (repopulation)**: to allow the regeneration of normal tissues to decrease the normal tissue injury.

IV. **Reoxygenation**: the hypoxic cells are radiation resistance. The reoxygenation shifts the cells to be more radiosensitive. Therefore the cells will be easier to be destroyed by radiation.

The fractionation schedule for adults is usually 1.8 to 2 Gy per day, five days a week until achieve the total dose. (5, 9)

Types of radiotherapy:

1. External radiotherapy or Teletherapy

   The ray is emitted from the source outside the body to the target.

   - Conventional external beam radiotherapy (2DXRT)

     Conventional external beam radiotherapy (2DXRT) is delivered via two-dimensional beams using linear accelerator machines. 2DXRT mainly consists of a single beam of radiation delivered to the patient from several directions. The treatment is planned or simulated on a specially calibrated diagnostic x-ray machine known as a simulator (2D). The problem of this technique is some high-dose treatments may be limited by the radiation toxicity capacity of healthy tissues which lay close to the target tumor volume. Physicians and physicists have limited knowledge about the true radiation dosage delivered to both cancerous and healthy tissue due to its two-dimensional limitation. For this reason, 3-dimensional conformal radiation therapy is becoming the standard treatment for a number of tumor sites.

   - 3-dimensional conformal radiation therapy (3DCRT)

     Using specialized CT and/or MRI scanners and planning software, the ability to analyze tumors and adjacent normal structures in three dimensions has improved. The profile of each radiation beam is shaped to fit the profile of the tumor, therefore the relative toxicity of radiation to the surrounding normal tissues is reduced, allowing a higher dose of radiation to be delivered to the tumor with normal tissue saving than conventional techniques.(14)

- Intensity-modulated radiation therapy (IMRT)

IMRT is an advanced type of high-precision radiation that is the next generation of 3DCRT. IMRT also improves the ability to conform the treatment volume to concave tumor shapes. The radiation dose intensity is elevated near the gross tumor volume while radiation among the neighboring normal tissue is decreased or avoided completely. This may result in better tumor targeting, lessened side effects, and improved treatment outcomes than 3DCRT. (15)

- Image-guided radiation therapy (IGRT)

IGRT allow much more precise radiation volume to the target tissues and decrease volume to the normal tissues. This is very useful since tumors can move between treatments due to differences in organ filling or movements while breathing. The tumor information is guided by specialized imaging tests, such as CT scans, ultrasound or X-rays. These tests are done along the motion cycle of the organ so IGRT is specific to the target's location, shape and motion characteristics. IGRT is suitable for the movable organ such as lung etc.(16)

In Thailand 2DXRT and 3DCRT are extensively used to treat many sites of tumors. IMRT is limited to use in only complicated body sites because it needs experienced medical personnel and only limited number of IMRT are available.

2. Brachytherapy

The radioactive material is inserted into the body near the target, and then the ray is gradually released to kill the cells. It is usually used as an effective treatment for cervical, prostate, breast, and skin cancer. (17)

3. Internal or systemic radiotherapy

The radioactive material is loaded into the body by intravenous or per oral techniques for example radioactive iodine or a radioactive substance bound to a monoclonal antibody. Radioactive iodine (^{131}I) is used to treat some types of thyroid cancer. A monoclonal antibody helps locate the radioactive substance to the right site and kill tumor cells. (18)

1.1.1 Oral cancer

The oral cancer is the malignant tumor that occurs in the oral cavity which involves lip, gingiva and alveolar ridge, buccal mucosa, retromolar trigone, tongue, hard palate and floor of mouth.

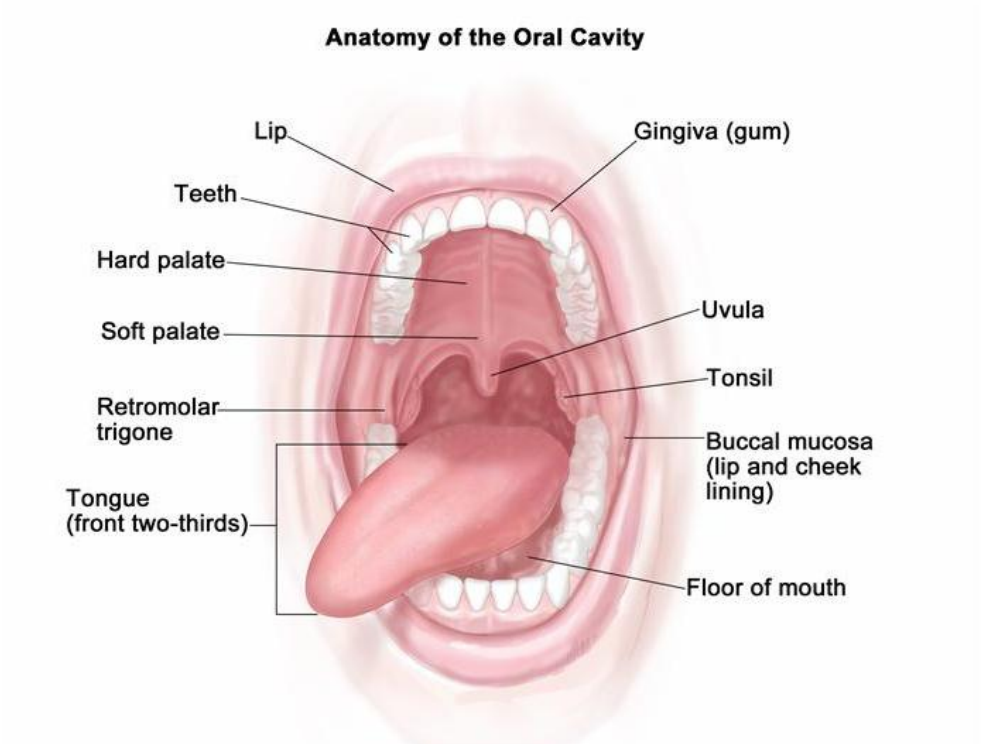


Figure 2 Anatomy of oral cavity

The oral cancer is the most common malignant tumor of the head and neck. The etiology of this cancer usually relates to genetic factors, alcohol consumption, betel nut chewing, poor oral hygiene, ill-fitting denture and tobacco use.

Treatment

The management of oral cancer is usually mainly by surgery, or combined with radiotherapy and chemotherapy. There are many factors that must be considered in treatment selection such as site, location, histology and stage of the tumors, nodes status including patients and physician factors.

Both surgical resection and radiation therapy are applicable, either singly or in combination. Surgical resection is the treatment of choice for patients with early-

stage tumors (T1 and T2). Radiotherapy alone is an alternative for patients who cannot tolerate surgery. Whereas advanced-stage tumors require combined-modality treatment for preferable outcome such as surgical resection combined with post-op radiotherapy. Chemotherapy alone does not increase survival rate so it may be combined with radiotherapy as adjuvant or neoadjuvant chemotherapy. (1, 19)

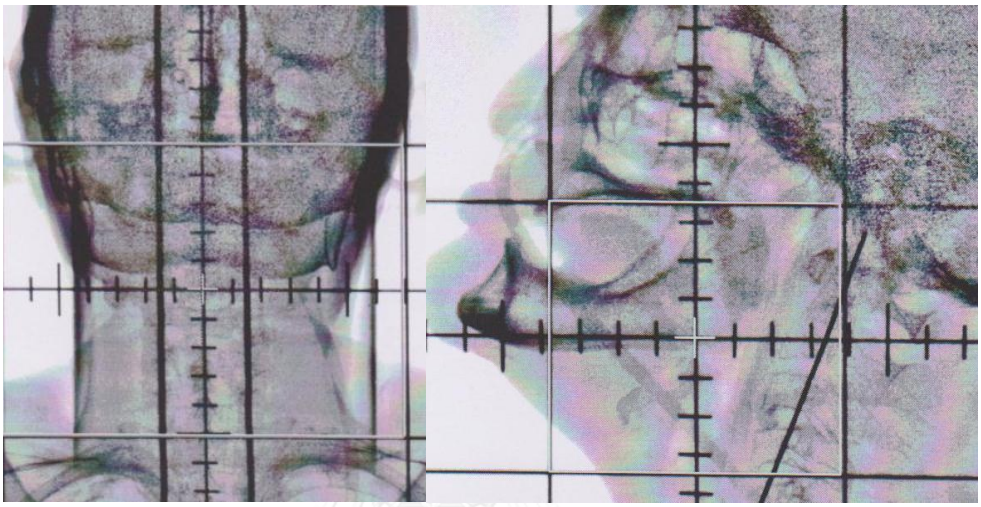


Figure 3 Radiation field of tongue cancer

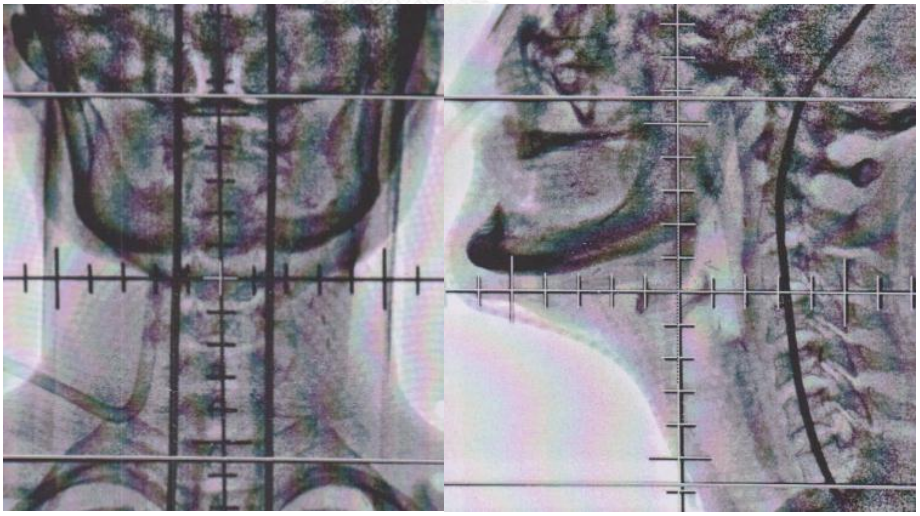


Figure 4 Radiation field of lower gum cancer

1.1.2 Oropharyngeal cancer

The oropharynx is located between the soft palate and the hyoid bone. The oropharyngeal cancer is the cancer which occurs from soft palate, tonsil, base of

tongue or lateral pharyngeal wall between the nasopharynx and the pharyngoepiglottic fold. The etiology of this cancer is similar to oral cancer

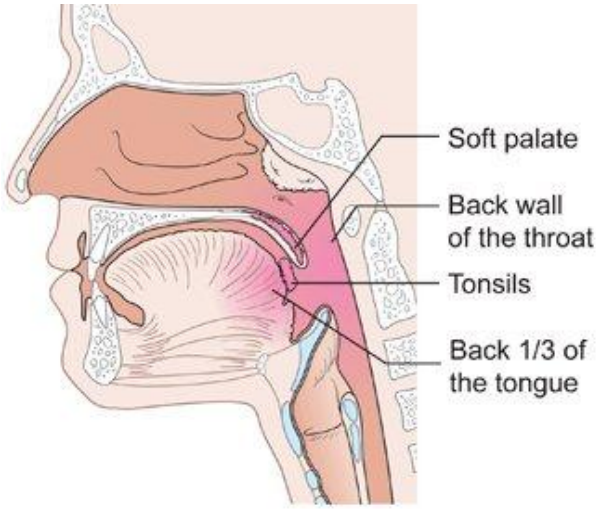


Figure 5 Anatomy of oropharynx

Treatment

In general early stage of the disease can be treated by either radiotherapy or surgery whereas a more advanced stage has to be treated by combination modality. Radiotherapy is more amenable than surgery because of its high rate of cure and its better outcome. Chemotherapy is reserved for a very advanced stage.(1)

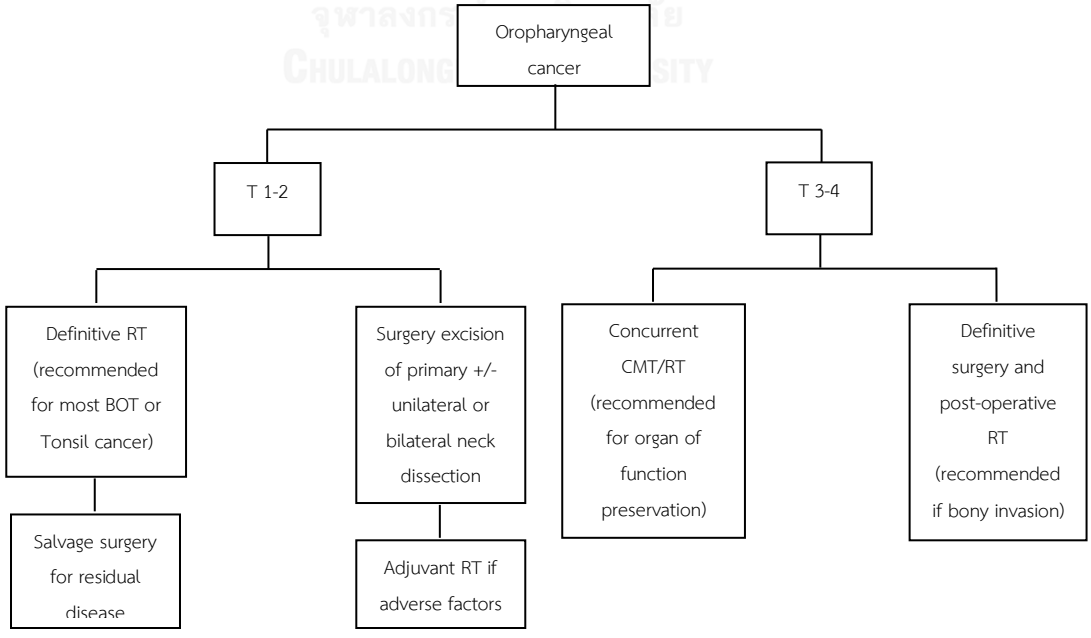


Figure 6 Demonstrate treatment modalities of oropharyngeal cancer (1)

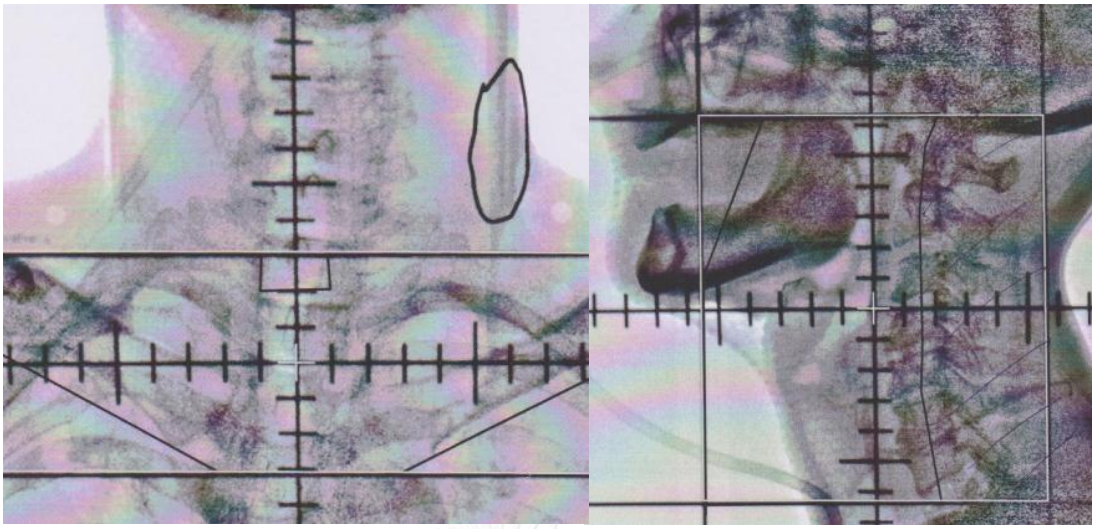


Figure 7 Radiation field of oropharyngeal cancer

1.2.1 Salivary gland cancer

Salivary glands include major salivary glands (parotid glands, submandibular glands, sublingual glands) and minor salivary glands. The major risk factors of salivary gland cancer are chewing tobacco, followed by smoking. Moreover older aged and radiation of head and neck area are also found to be the contributing factors.

Treatment

Surgery is the treatment of choice for salivary gland cancer. Radiotherapy is an adjunctive therapy. Occasionally, radiotherapy is used for the unresectable cases. Radiation alone is infrequently used for early disease. Chemotherapy is possibly helpful for palliation of an unresectable or recurrent disease. (1)

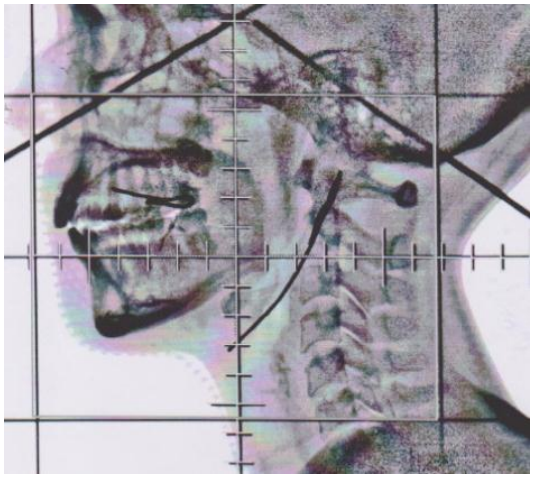


Figure 8 Radiation field of parotid gland cancer

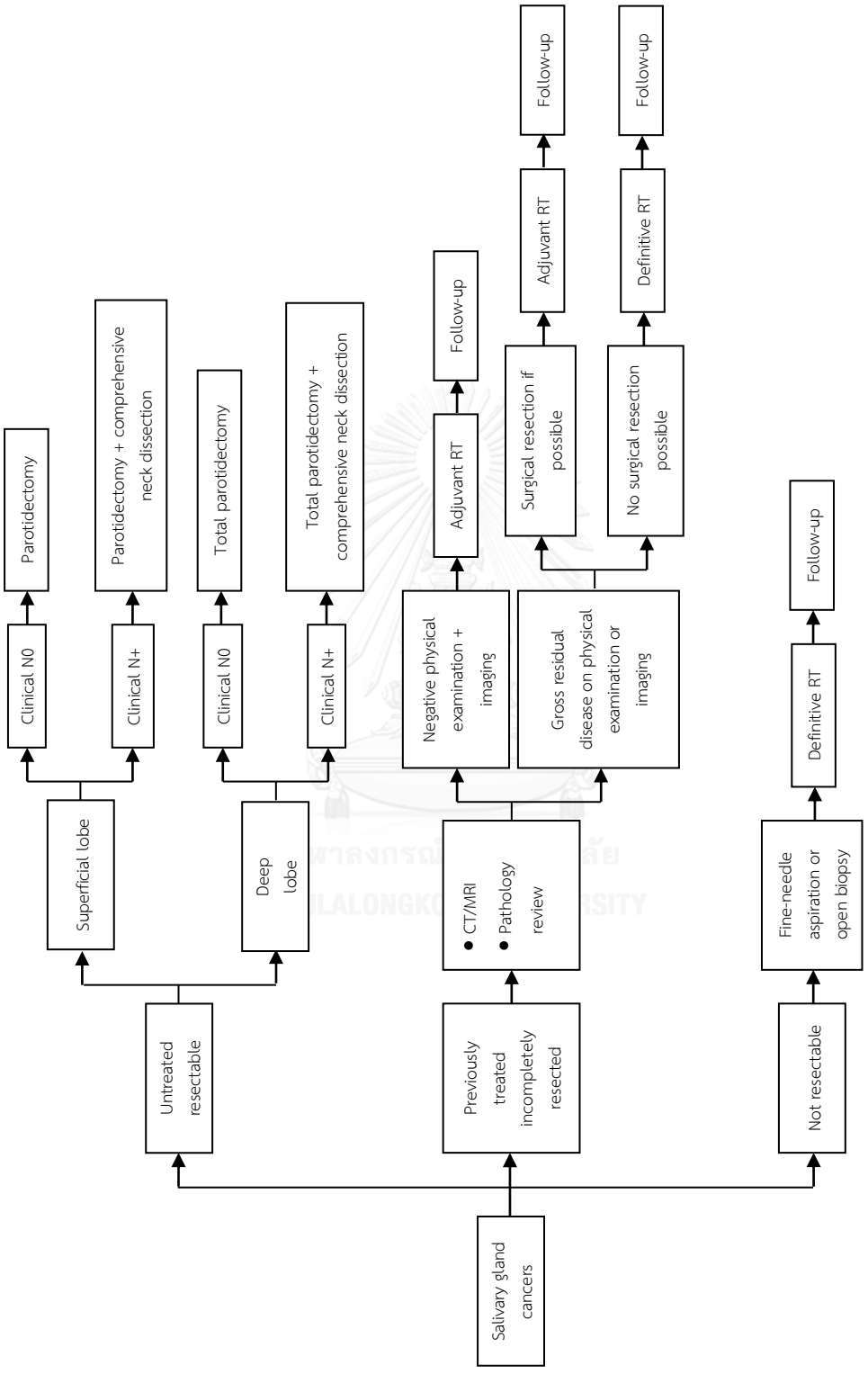


Figure 9 Demonstrate treatment modalities of salivary gland cancer (1)

1.1.4 Paranasal sinuses cancer

Sinonasal malignancies are rare. The most common type of these cancers is squamous cell carcinoma. Mainly the sinonasal cancers originate from maxillary sinus, nasal cavity and ethmoidal sinus respectively. A higher incidence is found in men older than 40 years old. Inhalation of some substances such as wood dust, aflatoxin, heavy metals, industrial chemicals, and leather tanning is assumed as the risk factors.

Treatment

Treatment is based on the location, stage, and histology of the disease. The contraindications to surgery are still controversial including involvement of the nasopharynx, clivus, and bilateral orbital cavities or optic nerves. Involvement of carotid arteries is relative contraindication to surgery. Extension to the critical structures such as brain or cavernous sinus is also unresectable. Early lesions may be treated with surgery alone. The patients with multiple systemic diseases are likely managed with radiotherapy alone. In the case of resectable advanced disease may be treated with surgery followed by radiotherapy. For unresectable tumors, chemotherapy or radiotherapy is the treatment of choice.(1)

1.1.5 Nasopharyngeal carcinoma

The nasopharynx is the upper portion of the pharynx that lies from base of skull to the soft palate, continuous with the oropharynx inferiorly. Anteriorly, it is open to nasal cavities. And posteriorly, it is lying against prevertebral fascia with a potential space, the retropharyngeal space, between. Its roof is formed by the body of the sphenoid bone.

At the lateral wall 1.5 cm posterior to the inferior nasal concha is the opening of the auditory tube (Eustachian tube) which leads to the middle ear. The base of the cartilaginous portion of the auditory tube lies directly under the mucous membrane of the nasopharynx, where it forms an elevation called the torus tubarius behind the pharyngeal orifice of the tube. Passing inferiorly from the posterior lip of the tubal opening is the salpingopharyngeal fold. The lining mucosa overlies the muscle, and posterior to the fold is pharyngeal recess (fossa of Rosenmuller). In the

roof and the posterior wall there is lymphoid tissue called the adenoid, or pharyngeal tonsil. (20-23)

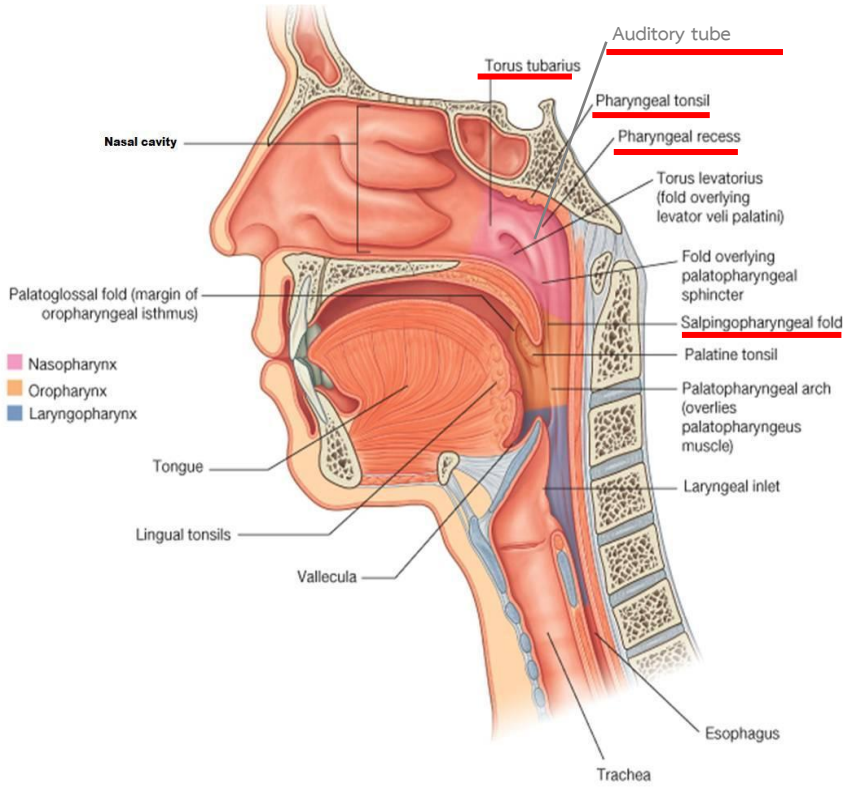


Figure 10 Anatomy of nasopharynx

Nasopharyngeal carcinoma (NPC) is an epithelial cancer that occurs in the nasopharynx.(23, 24) There are three main types of NPC reorganized in the World Health Organization (WHO) classification. (25)

1) Keratinizing squamous cell carcinoma: typically found in the older adult population
2) Non-keratinizing carcinoma
   a.) differentiated carcinoma
   b.) undifferentiated carcinoma
3) Basaloid squamous cell carcinoma: The rare aggressive subtype of squamous cell carcinoma.

NPC is usually occurs at the fossa of Rosenmuller (pharyngeal recess) due to its ideal ecological niche with suitable conditions for colonization of microorganisms. Some bacteria can produce fatty acid such as butyric acid which is known to increase

the reactivation of Epstein Barr virus in Raji cells and/or reduce nitrate to nitrite to form N-nitroso compounds.(26) Because of their location, most nasopharyngeal carcinomas remain asymptomatic for a long time. Palpable cervical lymph node metastases are the first sign of the disease in about half of the cases. The tumor does not form a large, space-occupying mass or extend into contiguous cavities. Rather it infiltrates neighboring regions, such as the parapharyngeal space through the pharyngobasilar fascia, orbit, and cranial cavity. (23)

The symptoms related with nasopharyngeal carcinoma include trismus, pain, otitis media, nasal regurgitation due to paresis of the soft palate, hearing loss and cranial nerve palsies. Larger mass may produce nasal obstruction or bleeding and a "nasal twang". The rich lymphatic network draining the nasopharynx is the route of frequent and early metastases to the cervical lymph nodes. Metastatic spread may result in bone pain or organ dysfunction. (23, 27)

It has been reported that the incidence is high in Southern China, South-east Asia, Arctic populations and tribes of North Africa.(28) It is the 2nd most common head and neck cancer (22.96%) in Thailand (2008) after oral cancer.(2, 29) The etiologies of this cancer appear to be multifactorial. There are evidences suggest that genetic, viral, and other environmental factors are involved similar to the head and neck cancer. Recent study found the correlation between nasopharyngeal carcinoma and a genetic factor which is a human leukocyte antigens (HLA) haplotype.(26)

Epstein – barr virus is strongly associated with the undifferentiated type (UNPC). Epstein – barr virus has been found in the tumor cells and β-lymphocytes of patients with nasopharyngeal carcinoma. Moreover, 85% of patients have antibodies to EBV and have anti-EBV IgA in the serum. But the exact mechanism of the pathogenesis of this tumor is still unknown.(8) There are many studies discovering the association between the Human Papilloma virus (HPV) and the type I nasopharyngeal carcinoma recently but more studies are needed to verify this finding. (30, 31)

Tobacco use and consumption of high levels of nitrosamine compounds diet, such as salted fish and preserved food etc., have moderate relationship with nasopharyngeal carcinoma, whereas vitamin A, coffee and green tea reduce risk of this disease. (32-34)

Treatment

Because of the anatomical structure of nasopharyngeal carcinoma and its tendency to involve cervical lymph nodes, it is difficult to perform surgery for local control. Biopsy of the involved lymph node is the routine surgical procedure. The nasopharyngeal primary tumor is rarely biopsied.(27)

Nasopharyngeal carcinoma is different from other head and neck cancers because of its association with Epstein-Barr virus, aggressive natural behavior with high prevalence for distant metastases, and particular therapeutic deliberation. Treatment is difficult due to anatomical proximity to critical structure but this cancer is radiosensitive and chemosensitive so the main treatments of this cancer are combined radiotherapy and chemotherapy.(35)

Due to its violence and limited radiosensitive characteristic, high dose of radiation is needed for complete eradication of nasopharyngeal carcinoma. A total dose of ≥ 70 Gy is needed even for T1-2 tumors. The general recommendation is to give 1.8 – 2 Gy daily fractions, five days a week to a total dose of 70 Gy to the gross tumor, and 50 – 60 Gy for elective treatment of potential risk sites.(35)

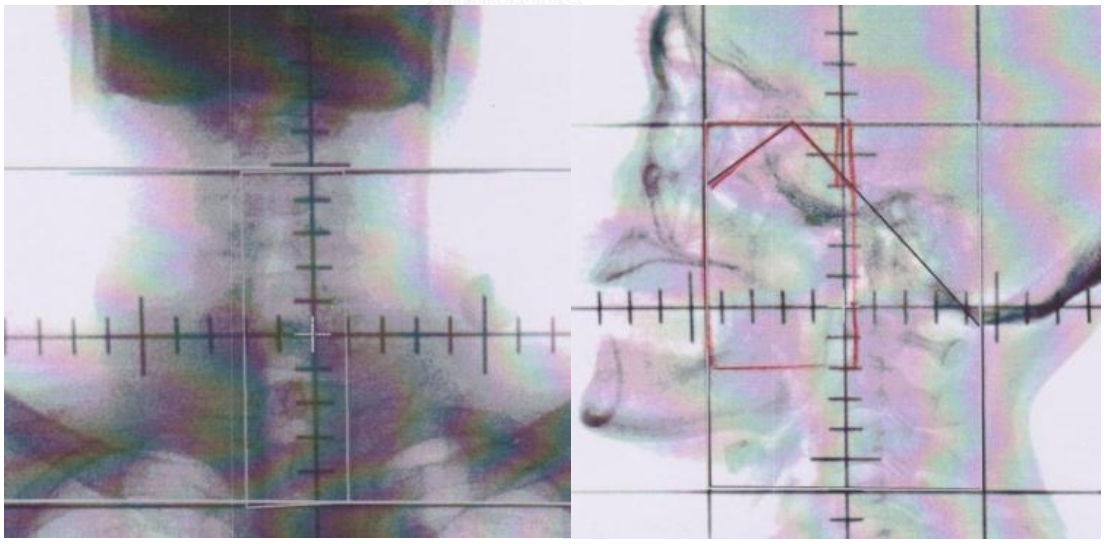


Figure 11 Radiation field of nasopharyngeal carcinoma

1.2 Oral complications of head and neck radiotherapy

The radiation affects not only the malignant cells but also the normal tissues within the radiation fields and leads to the several complications. The complications of radiotherapy depend on:

1. Dose of radiation : the complications are dose related. The severe side-effects occur when dose greater than 45 Gy are administered bilaterally to the mouth, jaws and salivary glands.
2. Total treatment time : the prolonged period of radiotherapy decreases the complications.
3. Field of treatment : if the area which receives the radiation is large, the more tissues or organs are affected.
4. Fraction : the advantages of radiation fractionation are allowing cells to reoxygenation and repair themselves during resting period and waiting for cells to enter the mitosis phase of cell cycle. (13)

The orofacial structures which may be affected by radiotherapy are the mucous membrane, salivary glands, taste buds, bone and teeth

1.2.1 Mucositis

The mucous cells are radiosensitive due to their high turnover rate and low radiation resistance. Daily treatment dose greater than 2 Gy suppresses the proliferative capacity of mucous membrane stem cells. As a result, most patients develop mucositis within the third week of radiotherapy. Oral mucosa becomes reddened because of the epithelium and vascular dilation, inflammation, and edema of the submucosa. Then the mucosa changes to peeling, ulcerated, and covered with fibrinous exudates. It usually appears together with pain, burning sensation and discomfort which negatively affect eating, swallowing and speech. It gradually recovers a few weeks after cessation of radiotherapy.

Figure 12 Radiation induced mucositis

1.2.2 Xerostomia

The ionizing radiation destroys the glandular tissue and leads to rapid, irreversible loss of salivary fluid secretion. As a result the salivary flow rate reduces and salivary composition changes. The acinar cells of parotid glands are more radiosensitive than the mucous cells of submandibular and sublingual glands. Receiving 2.25 Gy of radiation can produce a 50% reduction of resting flow rate within a day. Receiving 40 Gy of radiation may lead to permanent salivary gland injury and hyposalivation. The saliva quality and quantity may gradually recover over several months or may result in permanent grandular changes that cause irreversible loss of ability to secrete saliva. When quality and quantity of saliva decrease, its capacities are worse, such as buffering capacity, lubrication, antimicrobial effects, remineralization of teeth, digestive roles and maintenance of mucosal integrity. Subsequently inappropriate oral functions, burning sensation, cracked lips, and increased susceptibility to oral infections and increase the susceptibility of dental caries.

Figure 13 Radiation induced xerostomia (dry mouth)

1.2.3 Dysgeusia

Due to the radiosensitive characteristic of taste buds and the reduction of salivary flow, the dysgeusia occurs after receiving dose of 30 Gy. Mostly the severity of taste loss is partly restored 20-60 days after radiotherapy and is completely restored 2-4 months post-radiotherapy.

1.2.4 Radiation caries

The radiation affects the secretory mechanism of odontoblasts. The dental pulp decreases in vascularity also fibrosis. The teeth lose their ability of reparation and development. In addition the alterations of viscosity, buffering capacity, antimicrobial effects and remineralization of teeth due to hyposalivation promote the favorable environment for dental caries. The pattern of decayed tooth is different from general patients. The smooth surfaces of the teeth such as buccal and incisal aspect which normally are resistant to decay, are the first affected and the progression is rapid. This complication affects patients throughout their life.

Figure 14 Radiation caries

1.2.5 Osteoradionecrosis (ORN)

Osteoradionecrosis (ORN) is a condition of non-vital bone in a site of radiation injury longer than 3 months. The radiation causes the 3H effects to the bone: hypocellular, hypovascular and hypoxia, therefore the bone loses their reparative capacity and leads to cell death with or without infection. ORN can be spontaneous, but mostly resulted from tissue injury. Tooth extraction in irradiated jaws is the major risk factor of ORN. The mandible is much more affected than maxilla due to its poorer vascularization and higher bone density. The associated pain, trismus, suppuration, and pathologic fracture may also present.(5, 9, 36, 37)

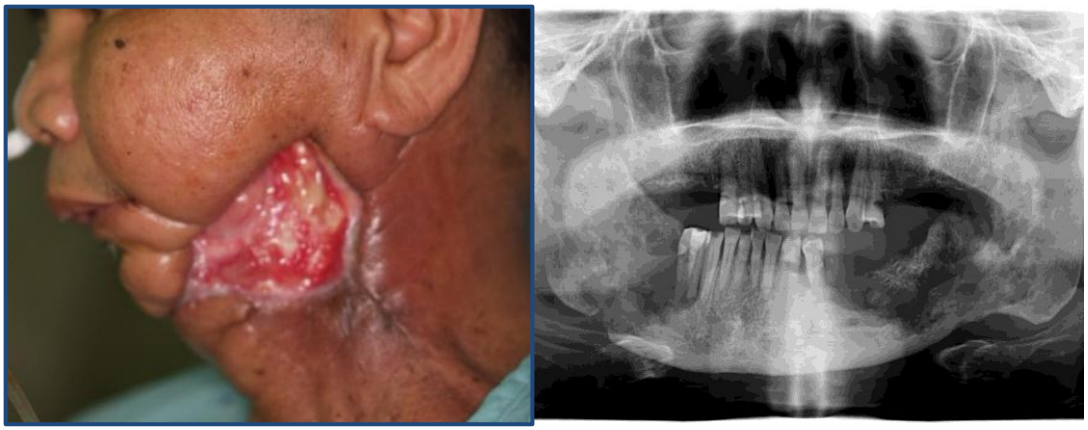


Figure 15 Osteoradionecrosis

1.2.6 Trismus

Radiation therapy for head and neck cancer which usually involves the temporomandibular joint, the pterygoid muscles, or the masseter muscles induces fibrosis in masticatory muscles and soft tissues of the cheek in the radiation field. As a result the reduction of the maximum mouth opening distance occurs and may lead to trismus. This complication likely cause difficulty in eating, maintenance of oral hygiene and wearing prosthesis, and then the nutritional deficiency and poor oral hygiene possibly happen. The patients' quality of lives after radiotherapy will become poorer. Furthermore the prevalence of trismus in irradiated head and neck cancer patients was rather high thus it is quite important and should be more concerned. (5, 9, 36, 38)

Figure 16 Radiation induced trismus

A complication related to the radiotherapy in head and neck cancer, which previously had not been paid much attention to, is trismus. However the prevalence of trismus in irradiated head and neck cancer patients was rather high and trismus may lead to other complications, thus it is very important and should be taken into consideration when treat these patients with radiotherapy.

1.3 Trismus

Trismus is the limitation of mouth opening less than individual normal range. It is also known as jaw hypomobility or locked jaw. There is no accurate criterion for trismus. In most studies trismus is diagnosed when the maximum mouth opening distance is less than or equal to 30 and 35 mm. in female and male respectively. However there are many factors affect the maximum mouth opening distance such as overbite, size of the body, and size of the jaws etc. Significant gender differences for maximum mouth opening distance were observed but no significant age differences were found. Although the maximum mouth opening distance is different individually but it is accurate and reliable when measurement is done in the same person especially by the same trained examiner.(39)

The cross-sectional study of Dijkstra et al. (2006) studied 89 head and neck cancer patients (13 dentate, 30 partially dentate, and 46 edentulous patients) who received cancer management by surgery or a combination of surgery and radiotherapy. The objective of their study was to identify the cut-off point for trismus in head and neck cancer patients. Maximum mouth opening distance of each patient was measured. The mandibular functional impairment questionnaires (MFIQ) were assessed. From the data, most patients had problems about jaws movement and were uncomfortable in their daily lives when their maximum mouth opening distance is lesser than 35 mm. Hence they concluded that a maximum mouth opening distance of less than 35 mm. is a functional cut-off point for trismus in head and neck cancer patients.(40)

Limitation of jaw opening may start abruptly or gradually. It affects both mental and physical health of patients because of pain and difficulties in daily activity for example eating, speaking, and oral hygiene maintenance. The severity of trismus can be evaluated from clinical examination and patients' complaint.

Figure 17 Radiation induced trismus

Etiology of trismus

Common causes of trismus are divided into 2 categories; intra-articular causes and extra-articular causes. (41-43)

1) Intra articular causes:
   - Fractured mandibular condyle or intracapsular fracture
   - Internal derangement of temporomandibular joint
   - temporomandibular joint dislocation
   - Traumatic synovitis
   - Septic arthritis
   - Osteoarthritis
   - Inflammatory arthritis (e.g. rheumatoid or psoriatic)
   - Ankylosis
   - Osteophyte formation
   - Etc.
2) Extra articular causes :
   - Trauma not involving the mandibular condyle
   - Post-surgical edema
   - Recent prolonged dental treatment
   - Following administration of inferior alveolar nerve block with local anesthetic (medial pterygoid muscle)
   - Hematoma of medial pterygoid muscle

- Acute infections of the oral tissues, especially involving the buccal space or muscles of mastication
    - Odontogenic infection
    - Peritonsillar abscess
    - Acute parotitis
    - Pericoronitis
    - Submasseteric abscess
- Tetanus
- Local malignancy
- Myofascial pain or temporomandibular joint dysfunction
- Radiation fibrosis
- Fibrosis from burns
- Submucous fibrosis
- Coronoid hyperplasia
- Malignant hyperpyrexia
- Drug associated dyskinesia
- Psychotic disturbances, hysteria
- Pain
- Etc.

Maximum mouth opening distance measurement

The maximum mouth opening distance (MMOD) can be measured by three methods including (41) :

1) **Maximum opening or maximum unassisted vertical opening**: patients are instructed to open their mouths as widest as they can without consideration of pain.
2) **Maximum comfortable opening or maximum unassisted vertical opening without pain**: patients are instructed to open their mouths as widest as they can without pain
3) **Maximum assisted opening**: the examiner helps patients to open their mouth.

If no pain involved, the maximum mouth opening distance from method 1 and 2 are not different. Method 1 and 2 are called “active opening” (unassisted opening) and method 3 is called “passive opening” (assisted opening).

The maximum mouth opening distance was commonly measured from incisal edge of upper and lower central incisor (Maximum interincisal distance or MID) plus overbite. There are several tool of measurement, for example, ruler, vernier caliper, and Therabite™ range of motion scale.

Trismus can lead to other dental complications because it may result in difficulties with daily activities such as eating, chewing, swallowing, breathing, speaking and maintenance of oral hygiene. When the patients have trismus, they will have the problems with oral hygiene care and dental treatment, leading to poor oral health and poor quality of lives. To treat trismus after receiving radiation is extremely difficult with poor result. Therefore, the prevention and alleviation of trismus will decrease these complications and improve the patients’ quality of lives.(44-47)

Treatment

Treatment of trismus varies depending on the etiology factors. The trismus therapy includes heat therapy, physiotherapy (jaw exercise), electrotherapy, medicine therapy, and surgical procedure. The appropriate treatment is to eliminate the causes. Therefore, diagnostic assessment should be done before treatment.(38, 48-51)

Research objectives

To compare the effects on maximum mouth opening distance between dynamic and static jaw exercise in irradiated head and neck cancer patients.

Research Question

Do the applications of dynamic and static jaw exercise differently affect the maximum mouth opening distance in irradiated head and neck cancer patients?

Hypothesis

Null hypothesis (H_0) : The effects on maximum mouth opening of dynamic and static jaw exercise in irradiated head and neck cancer patients are *not different*.

Alternative hypothesis (H_1) : The effects on maximum mouth opening of dynamic and static jaw exercise in irradiated head and neck cancer patients are significantly *different.*

Research design

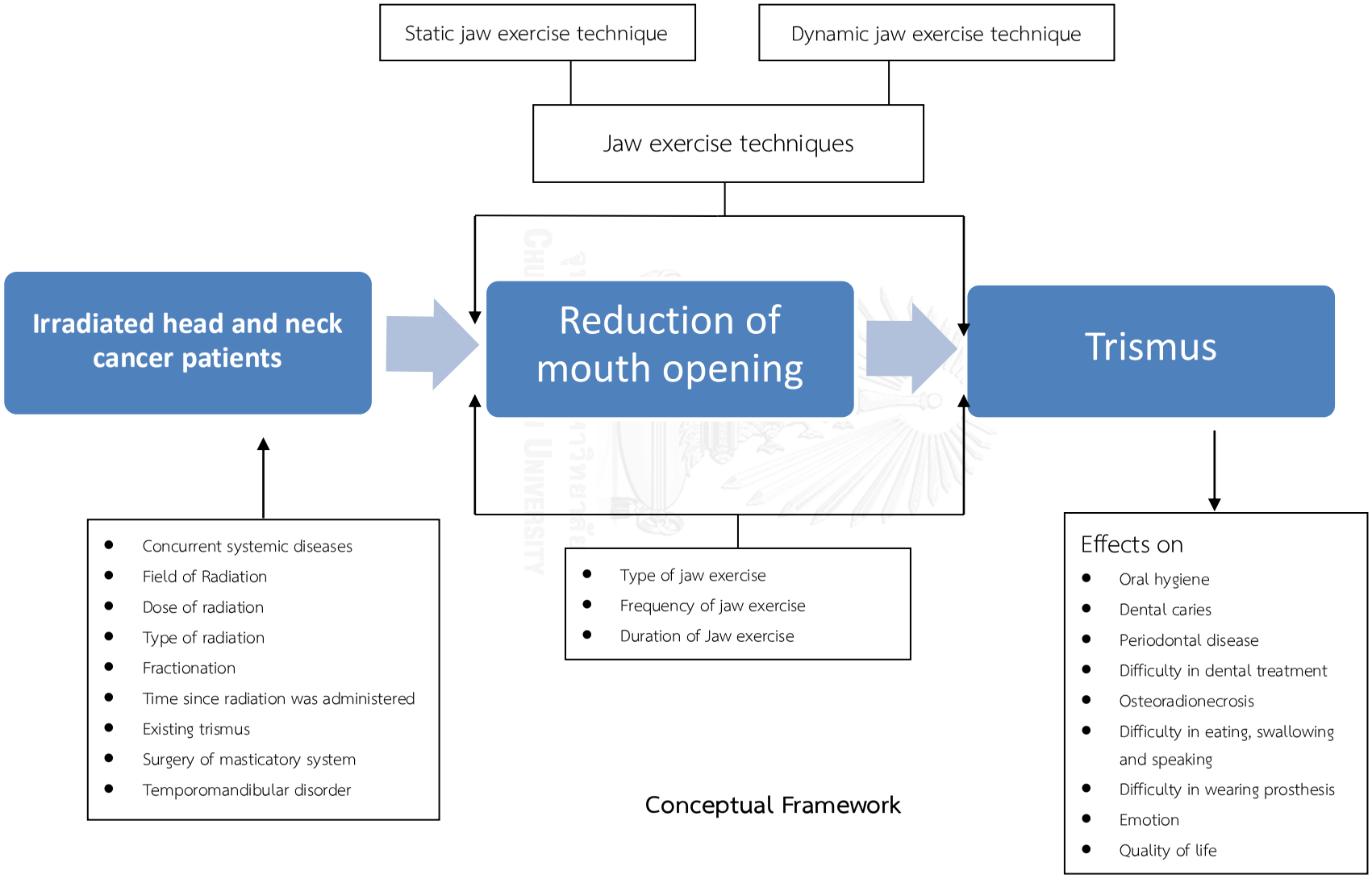
A randomized prospective clinical study

Expected benefits

1. To obtain a guideline for prevention and management of trismus in patients receiving radiotherapy for head and neck cancer.
2. Improving the jaw exercise technique and apparatus for this group of patients.
3. To improve the quality of lives and oral hygiene of post-radiotherapy patients.
4. Dentists can render a better dental care for these patients.

Key words

Head and neck cancer, Radiotherapy, Trismus, Static jaw exercise technique, Dynamic jaw exercise technique, Maximum mouth opening distance



Conceptual Framework

Chapter 2
Review of literatures

Radiotherapy for head and neck cancer causes the reduction of the maximum mouth opening distance and may lead to trismus. Radiotherapy involving the temporomandibular joint, the pterygoid muscles, or the masseter muscles is most likely to cause trismus. The radiation induced fibrosis in masticatory muscles and soft tissues of the cheek in the radiation field.(44, 52) Trismus likely occurs when muscles receive excess radiation dose of 40 Gy and the prevalence increases with increasing dose.(53) If the radiation dose of every 10 Gy is further received, the probability of trismus will increase by 24%.(54)

The radiation incurs injury of the tissues and then the inflammatory response is stimulated. The inflammatory cells e.g. monocytes, macrophage and platelet, are activated and accumulate at the injured tissues secreting cytokines and growth factors. The radiation tissue injury is a result of both the direct effects of the radiation on the cells and the inflammatory response. The cytokines and growth factors induce fibroblast aggregation and proliferation. The secretion of extracellular matrix by fibroblast increases while the degradation decreases especially the collagen fibers. As a result the fibrosis of the tissues in the radiation field occurs and limitation of jaw opening follows.(52, 55) The severity of the fibrosis depends on types of radiotherapy, radiation fields, dose of radiation, fractionation and time since radiation was administered.(44) The radiation dose to neuromuscular structures (especially the dose to masseter and pterygoid muscles) affects the maximum mouth opening distance more predominantly than the dose to temporomandibular joint.(46, 55, 56) Initially, it begins with loss of tissue elasticity followed by induration. Receiving a further dose of radiation, a greater degree of injury happens. The tissues become more indurate, rigid and retracted related to fibrosis of the dermis and subcutaneous tissue. As a consequence the restriction of the jaw opening befalls and maximum mouth opening distance decreases leading to trismus.(52)

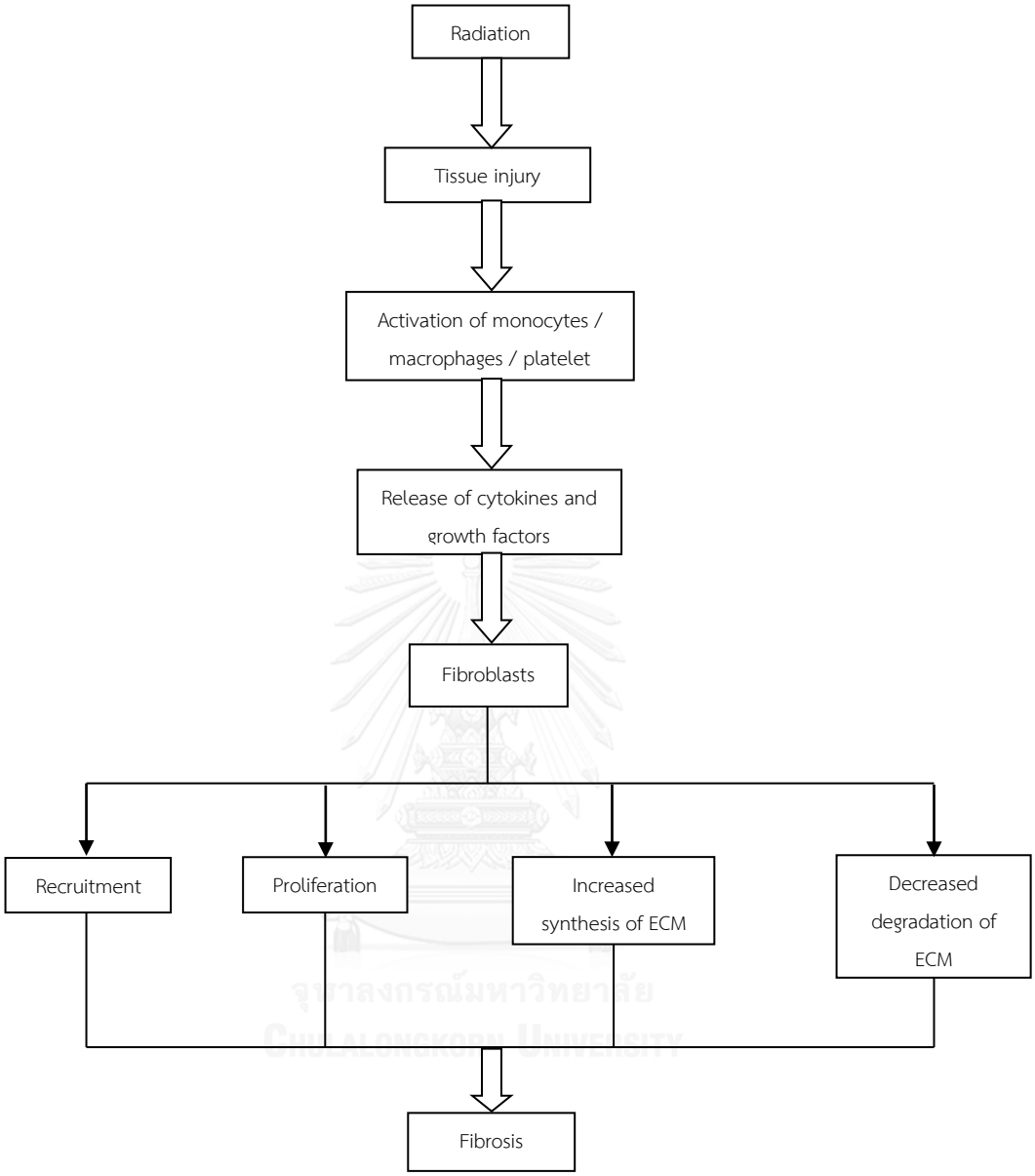


Figure 18 Demonstrate the process of soft tissue fibrosis due to head and neck radiotherapy(52)

Chon-Jong Wang et al. (2005) measured the degree of trismus induced after radiotherapy for nasopharyngeal cancer and assessed its progress over time. This study was a prospective, single-armed measurement study with long-term follow-up. Seventeen nasopharyngeal carcinoma patients treated with radiotherapy were studied for 4 years. The maximum interincisal distance (MID) started to decrease

within the first week of radiation and the rate is directly proportional to the time since radiation was administered. During the 9 weeks of radiotherapy there was no significant change of MID (1.3% per month). The rate of decrease turned into rapid at 1-9 months post-radiotherapy (2.4% per month) and then became slower and prolonged over the last 3 years (0.2% per month during 12-24 months and 0.1% per month during 24-48 months after radiotherapy). The total mean of MID decrease at 4 years after radiotherapy was 3.2%.(57)

Similar to the study of Chen et al. (2011) revealed the rate of maximum mouth opening distance reduction of the nasopharyngeal carcinoma patients during the first 6 months after receiving IMRT was remarkable (0.9% per month), then slowed down and started to be stable 1 year after radiotherapy.(58) Wetzels et al. (2014) showed that the reduction of maximum mouth opening distance occurred shortly after treatment and then partly restored within 6 months which was stable throughout 1 year.(59)

Regarding the results of several previous studies, most revealed that the prevalence of trismus in irradiated head and neck cancer patients was high (38-47%).(45, 46, 60) The prevalence of the patients who received conventional radiotherapy (25.4%) was much higher than the patients who received IMRT (5%).(61) While chemotherapy does not affect trismus.(46)

Dijkstra et al. (2007) analyzed the number and type of jaw exercise as well as the mouth opening before and after exercise therapy from the medical records of 37 patients with the diagnosis of trismus. 29 patients were diagnosed trismus related to head and neck cancer and 8 patients with trismus not related to cancer. Jaw exercise included active range of motion exercise, hold relax techniques, manual stretching and joint distraction. The mean number of treatments given to both group were not different significantly. The increase of mouth opening in the group of patients with trismus related to head and neck cancer was less than the other group significantly. They concluded that the trismus related to head and neck cancer is more difficult to treat with exercise therapy than the trismus from other causes. Once fibrosis of the masticatory muscles occurred, it was hard to stretch. Therefore the prevention of trismus is better than treatment.(47) Furthermore trismus possibly turns into severe

in most cases. Delayed treatment may cause the secondary change to both muscles and joints and agitate the recovery. Thus the jaw exercise should be initiated as soon as possible to retard the progression of trismus.(62)

Paul et al. (2012) assessed the impact of trismus on health related quality of life (HRQL) in head and neck cancer patients by evaluating the patients before and after cancer treatment. 75 patients with a diagnosis of head and neck cancer which expected to develop trismus were collected. The maximum interincisal distances (MID) of the patients were measured and the patients answered questionnaires about quality of life (health-related quality of life – HRQL, EORTC QLO C30, EORTC QLO H&N 35, Gothenburg Trismus Questionnaire – GTQ, and the Hospital Anxiety and Depression Scale – HADS). The data were collected before treatment and then at 3, 6, 12 months after finished the oncologic treatment. They used the MID ≤ 35 mm. as a criterion for trismus. They found that the patients had impairment towards mouth opening and jaw-related problems, problems with dry mouth and swallowing, eating limitations, muscular tension and pain after oncologic treatment consistent with the incidence of trismus. They concluded that trismus not only affected the patients' daily life activities but also the social lives and the ability to work. Besides, pain related to trismus was frequently associated with depression, anxiety and insomnia. Shortly, trismus negatively affected the quality of life after oncologic treatment of the patients.(60)

Most studies about trismus after irradiation of head and neck cancer revealed the prevalence about this complication, few focused on management and none of them mentioned prevention. There are some options for management of trismus such as medication therapy, electrotherapy and physiotherapy.

Some drugs have a role in the trismus management. Pentoxifylline is a methylxanthine derivative. It improves microcirculation and tissue oxygenation. It also reduces some cytokines which have been proved to play a significant role in the pathogenesis of radiation-induced fibrosis including tumor necrosis factor, interleukin-1, interleukin-6, and TGF-β. Daniel et al. (2001) studied 16 nasopharyngeal carcinoma patients with severe trismus (MID ≤ 25 mm.) developed after radiotherapy. The patients were given pentoxifylline orally at a dose of 400 mg. 2-3 times per day for 8

weeks. The MID were improved significantly (mean of increasing MID = 4 mm. with a range of 2-25 mm.). However pentoxifylline has side effects such as nausea and vomiting, dizziness, diarrhea, blurred vision and jaundice etc. and it cannot be used in the patients allergic to pentoxifylline.(49)

In addition the impedance-controlled microcurrent was used for management complications in irradiated head-and-neck cancer patients. Arlene et al. (2002) evaluated the effectiveness of impedance-controlled microcurrent therapy for treatment of sequelae in head-and-neck cancer patients. The patients had completed radiotherapy at least 6 months before participating the study. The patients were administered microcurrent 0.5 to 100 Hz treatments twice a day for 5 days with a variety of physical treatment such as massage, heat, and physical manipulation according to their insurance. No additional physical therapy or electrical stimulation was allowed during the follow-up period. 3 months after the end of microcurrent the jaw opening increased 4.6 ± 2.2 mm. on average. Besides, the cervical rotation, the cervical extension or flexion, and the cervical lateral flexion are also improved.(63) However it is not practical for most patients coming to the hospital treated with microcurrent every day.

Nowadays, there are several jaw exercise appliances and techniques which are effective in management of trismus e.g. Sledgehammer, surgical mouthprop, tapered screw, screw-type mouth gag, fingers, Therabite®, tongue blade stack, fabricated self-curing bite block, interarch springs, and Dynasplint.(48, 64, 65) They may be divided into 2 categories; the dynamic appliances and the static appliances. But there have been no clear clinical practice guidelines for the prevention or management of trismus.

Figure 19 The sledgehammer used for treatment of trismus

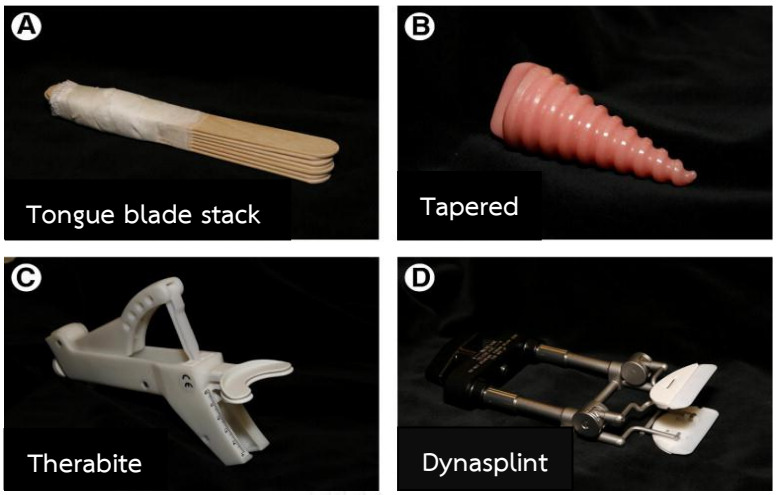


Figure 20 Jaw exercise appliances A) Tongue blade stack B) Tapered screw C) Therabite® D) Dynasplint

The dynamic jaw exercise techniques are the exercise that activate jaw opening and closing more than 1 cycle at one time of jaw exercise such as the TheraBite® Jaw Motion Rehabilitation System™. While the static jaw exercise techniques activate only 1 cycle at one time for example the tongue blade stack.

One of the widely-used jaw exercise appliances is the Therabite®. Currivan et al. (1993) compared the TheraBite® Jaw Motion Rehabilitation System™ with tongue blade stack as a technique for trismus management in 5-year or more post-radiotherapy patients. All the 21 patients have maximum interincisal distance (MID) of 30 mm. or less. The patients were divided into 3 groups randomly. The 5 patients in group 1 were instructed to exercise 10 sessions each day by finger-forced opening. The 7 patients in the tongue blade stack group (group 2) and the 9 patients in the Therabite® group (group 3) were instructed to use the tools five times each session, holding each stretch for 30 seconds, 6-10 sessions per day. After 10 weeks, the increase in MID between the finger-forced exercise group and the tongue blade therapy group were not different significantly. Meanwhile the MID in the Therabite® group was improved 2.6 times faster than the other groups. They concluded that the use of Therabite® increased the MID more than tongue blade stack significantly. However the sample size of the study was relatively small and the regimens of each

group were the same (dynamic applications). Their study was designed for trismus management not prevention.(66)

The Therabite® is one of the dynamic appliances and was proved to be more effective than several other appliances. Unfortunately the Therabite® is not sold in Thailand and it is very expensive. The fingers application and the tongue blade stack were considered as the useful jaw exercise technique and appliance and widely used for most patients.(65, 66) However there has been no study of jaw exercise by tongue blade stack compared with fingers forced mouth opening with different exercise techniques.

From the searching of previous study there is no study comparing the efficacy of trismus prevention between dynamic and static jaw exercise techniques in irradiated head and neck cancer patients. None of them focused on preventing radiation-induced trismus even though the prevention is better than treatment.

This study was designed to compare the effects on maximum mouth opening between dynamic and static jaw exercise to prevent trismus in irradiated head and neck cancer patients. The fingers forced mouth opening represents for the dynamic jaw exercise and the tongue blade stack represents the static one because they are readily affordable for most patients and widely used in Thailand.

Chapter 3
Materials and methods

3.1 Samples

66 Head and neck cancer patients both male and female ages ranged from 20 to 75 who received external beam radiation therapy through masseter muscles, pterygoid muscles or temporomandibular joint with or without chemotherapy from Chonburi Cancer Hospital were included in the study. The dose ranged from 50 – 70 Gy with fractionated dose of 1.8 – 2.0 Gy per day, five days a week. No operation was done through masticatory apparatus.

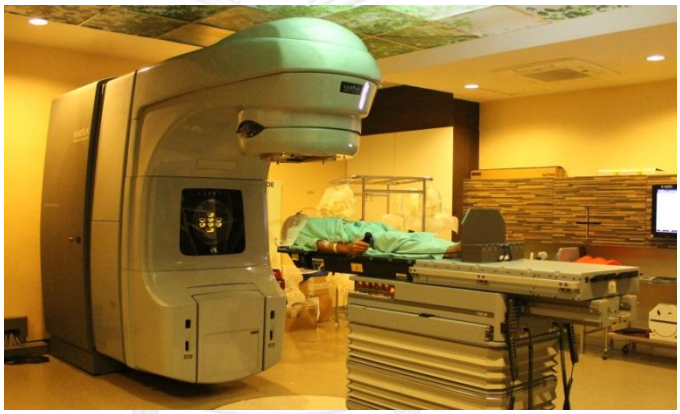


Figure 21 External beam radiotherapy of head and neck cancer

Exclusion criteria

1. Patients who could not perform jaw opening exercise as assigned such as patients with hand muscles weakness, patients with disabilities and patients with neurological defects etc.
2. Patients who received prior radiotherapy on head and neck region.
3. Patients who underwent masticatory muscles or temporomandibular joint surgery.
4. Patients who could not enroll throughout the study
5. Patients whose treatment plan were changed to surgery.
6. Patients with cancer involved masticatory muscles, temporomandibular joint
7. Non-compliant patients

Samples were divided into 2 groups by simple random sampling (drawing). 33 patients were in the static jaw-exercise technique group and the other 33 were in the dynamic jaw-exercise technique group.

3.1.1 Static jaw-exercise technique group

The patients were instructed to insert a stack of the tongue blade sticks until obtain the maximum mouth opening distance of each patient into one side of their mouth between the upper and lower posterior teeth for 2 minutes, 5 times daily (before tooth brushing, before each meal and before bedtime). In cases of no posterior teeth the stack was wrapped by a piece of clean cloth and place it on one side of the mouth between the posterior upper and lower edentulous ridge. (**Figure 22)**

Figure 22 Demonstrate jaw exercise with tongue blade stack (static group)

3.1.2 Dynamic jaw-exercise technique group

The patients were instructed to place their own thumbs at the upper anterior teeth or alveolar ridge and index fingers at the lower anterior teeth or alveolar ridge and then stretch the upper and lower arch forcefully (scissors-like action) until the maximum mouth opening is obtained. Hold the stretch for 30 seconds then close their mouth in the rest position for 30 seconds (1 cycle). Repeat the exercise for 5 sessions each day, with 4 cycles within each session (before tooth brushing, before each meal and before bedtime). **(Figure 23)**

Figure 23 Demonstrate jaw exercise with fingers (dynamic group)

3.2 Methods

1. Patients participating in the study were informed about the process, the conditions, the benefits and disadvantages of this study and informed consent were obtained from each patient in the study.
2. The distance of maximum mouth opening (active opening) of the patients was measured in millimeters using the disposable Therabite™ range of motion scale (Atos Medical, Sweden) before receiving the first radiotherapy by measuring from the incisal edge of upper central incisor to the incisal edge of opposing lower central incisor while the patients opened their mouth as widest as they can, then recorded the distance plus overbite. In case of patients lost both upper and lower central incisors the measurement was made between the opposing upper and lower lateral incisors. If the patients lost their upper central incisor, the distance between the alveolar ridge of maxilla and the opposing incisal edge of lower central incisor was measured. In patients losing their lower central incisor, the distance between incisal edge of the upper central incisor and the opposing alveolar ridge of mandible was recorded. In patients who lost both upper and lower anterior teeth the measurement was made between the midline of upper and lower alveolar ridge. **(Figure 24)**

Figure 24 Demonstrate the measurement of maximum mouth opening distance (MMOD) by the Therabite™ range of motion scale

3. The patients exercised according to the jaw exercise protocols of each group.
4. The patients were followed up and motivated, also the maximum mouth opening distance was measured every two weeks during radiotherapy course (week 2, 4, 6) and in the last day of radiotherapy.
5. After radiotherapy the patients continued the jaw exercise and the maximum mouth opening distance was measured at 1st, 3rd, and 6th month post-radiotherapy.
6. The patients answered the questionnaire about their quality of lives and compliance with jaw exercise technique at the last follow-up day (6th month after radiotherapy)
7. Compared the maximum mouth opening distance change between pre-treatment and 6 month post-treatment.

Data analysis

Statistical analyses were determined using the Statistical Package for the Social Sciences software (SPSS) version 17.0 (SPSS Inc., Chicago).The level of significance for all statistical test was set at α= 0.05. The percentage of maximum mouth opening distance change was determined and presented as mean ± SD and range. Statistical comparison of percentage of maximum mouth opening distance change dynamic and static jaw exercise was performed using independent t-test.

Chapter 4
Results

Part I: Demographic information

66 Head and neck cancer patients who received external beam radiation therapy through masseter muscles, pterygoid muscles or temporomandibular joint with or without chemotherapy from Chonburi Cancer Hospital were randomly divided into 2 groups equally: the static group and the dynamic group. The static group consisted of 33 patients. 14 patients had to be excluded: 5 were non-compliant patients, 6 patients refused radiotherapy due to intolerance to pain, 1 patient withdrew from the study 1 month after radiotherapy, 2 died during the study (1 patient died during radiation and the other died 1 month post radiotherapy).The 19 remaining patients were 7 females (36.8%) and 12 males (63.2%) with a mean age of 54.4 ± 14.6 years (26 – 75 years). 16 patients received chemo-radiotherapy (84.2%) and 3 were treated with radiotherapy only (15.8%). Most of them were irradiated with conventional external beam radiation therapy (2DXRT) (11 patients, 57.9%) and the rest of them were treated with IMRT (8 patients, 42.1%). All of them never had surgery involved the masticatory apparatus. **(Table 2)**

The dynamic group consisted of 33 patients. 13 patients were excluded: 1 was non-compliant patients, 5 refused the radiotherapy because of pain, 1 patient withdrew from the study during the course of radiotherapy, 5 died during the study period (2 patients died during radiation and the others died 1 month post radiotherapy), one was changed to undergo surgery. The 20 remaining patients were 3 females (15%) and 17 males (85%) with a mean age of 53.8 ± 10.6 years (28 – 75 years). 19 of 20 patients received chemo-radiotherapy (95%) and only one was treated with radiotherapy only (5%). Most of them were irradiated with conventional external beam radiation therapy (2DXRT) (15 patients, 75%) and the rest of them were treated with IMRT (5 patients, 25%). All of them never received surgery involved the masticatory apparatus. **(Table 3)**

Table 2 The demographic information of the patients in the static group

Variables	Mean (SD)	Range	Percentage (n)
Age (years)	54.4 (14.6)	26–75	
Radiation dose (cGy)	6,625.8 (539)	5,000–7,000	
Gender			
Male			63.2% (12)
Female			36.8% (7)
Tumor type (n=19)			
Squamous cell carcinoma			84.2% (16)
Adenoid Cystic Carcinoma			10.5% (2)
Mucoepidemoid carcinoma			5.3%(1)
Tumor site (n=19)			
Base of tongue			26.3% (5)
Nasopharynx			31.6% (6)
Tonsil			10.5% (2)
Tongue			10.5% (2)
Parotid gland			15.8% (3)
Lower gum			5.3% (1)
Stage of tumor			
I			5.3% (1)
III			21%(4)
Iva			68.4% (13)
Ivb			5.3% (1)
Type of radiation			
2DXRT			57.9% (11)
IMRT			42.1% (8)
Chemotherapy			
Yes			84.2% (16)
No			15.8% (3)
Pre-treatment MMOD	47.32 (9.91)		
6 months post-treatment MMOD	44.32 (8.84)		

Table 3 **The demographic information of the patients in the dynamic group**

Variables	Mean (SD)	Range	Percentage (n)
Age (years)	53.8 (10.6)	28–75	
Radiation dose (cGy)	6,840 (321.84)	6,000–7,000	
Gender			
Male			85% (17)
Female			15% (3)
Tumor type (n=20)			
Squamous cell carcinoma			95% (19)
Not identified			5% (1)
Tumor site (n=20)			
Base of tongue			5% (1)
Nasopharynx			45% (9)
Tonsil			10% (2)
Tongue			5% (1)
Larynx			5% (1)
Retromolar trigone			5% (1)
Pyriform			5% (1)
Floor of mouth			10% (2)
Oropharynx			10% (2)
Stage of tumor			
III			40%(8)
Iva			35% (7)
Ivb			25% (5)
Type of radiation			
2DXRT			75%(15)
IMRT			25%(5)
Chemotherapy			
Yes			95% (19)
No			5%(1)
Pre-treatment MMOD	47.9 (12.19)		
6 months post-treatment MMOD	43.45 (12.92)		

Part II: Study the effects of jaw exercise techniques on maximum mouth opening distance

The average maximum mouth opening distance of most patients started to decrease after the 2nd week during radiation treatment because of radiation induced pain and the symptom gradually decreased 1 month after treatment and then dropped again afterward as shown in **figure 25**.

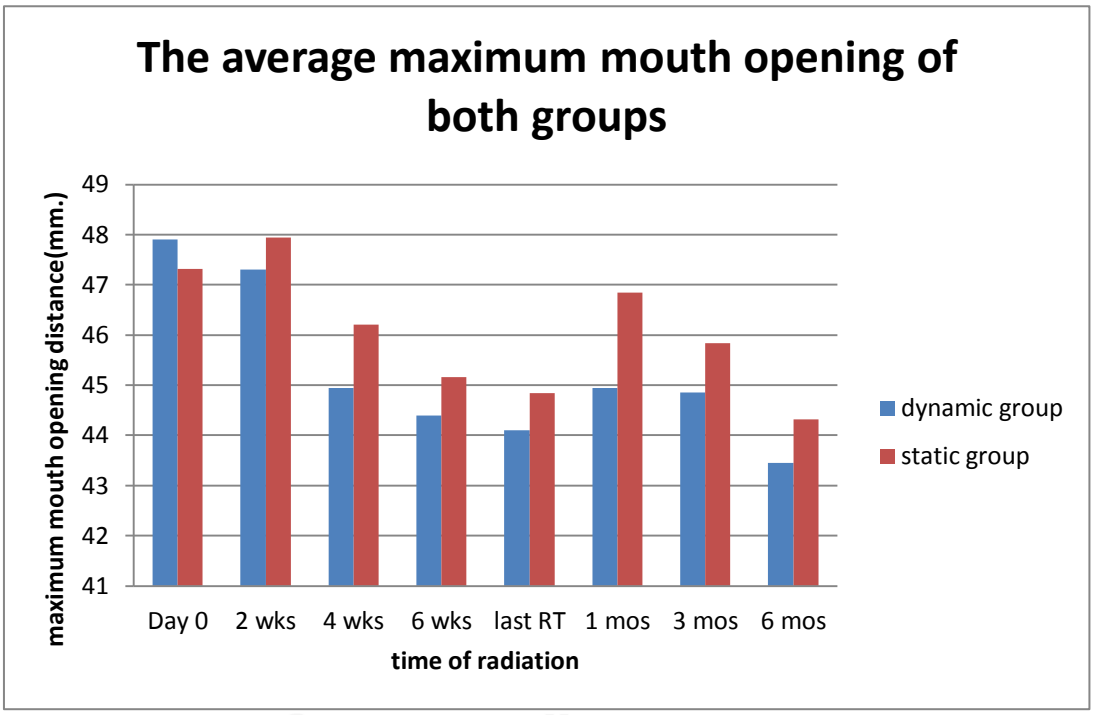


Figure 25 Demonstrate the average maximum mouth opening distance change during and post-radiotherapy

For the static group (19 patients) at six months after radiotherapy, the maximum mouth opening distance of 5 patients (26.3%) increased, 2 patients (10.5%) were not changed, while the others' (63.2%) decreased compared to the pre-treatment data. The average percentage of the maximum mouth opening distance of the static group decreased 4.55% (SD = 18.84%).

For the dynamic group (20 patients) at six months after radiotherapy, the maximum mouth opening distance of 5 patients (25%) increased and the others' (75%) deceased compared to the pre-treatment data. The average percentage of maximum mouth opening distance of the dynamic group decreased 9.58% (SD = 13.89%).

The average percentage of the maximum mouth opening distance reduction of the dynamic group was more than those of the static group but not statistically significant (p = 0.347). **(Table 4)**

Table 4 Demonstrate the average percentage of the maximum mouth opening distance change of both groups

Group	Number of patients	Average percentage of MMOD change at 6 months post-RT compared to Pre-RT	
		Mean (SD)	Range
Static	19	-4.55 (18.84)	(-)29.82 – (+)51.43
Dynamic	20	-9.58 (13.89)	(-)28.89 – (+)17.24

There was an outlier whose was female aged 41 in the static group with nasopharyngeal carcinoma and received IMRT concurrent with chemotherapy. Her initial MMOD was 35 mm. and went up to 53 mm. at 6 months post-radiotherapy. The percentage of MMOD change was 51.43% **(Figure 26)**. If excluded the outlier, the average MMOD change of the static group at 6 months post-radiotherapy compared to pre-radiotherapy was 7.66% reduction (SD = 13.47%). It was not significant different from those of the dynamic group (p = 0.668). **(Table 5)**

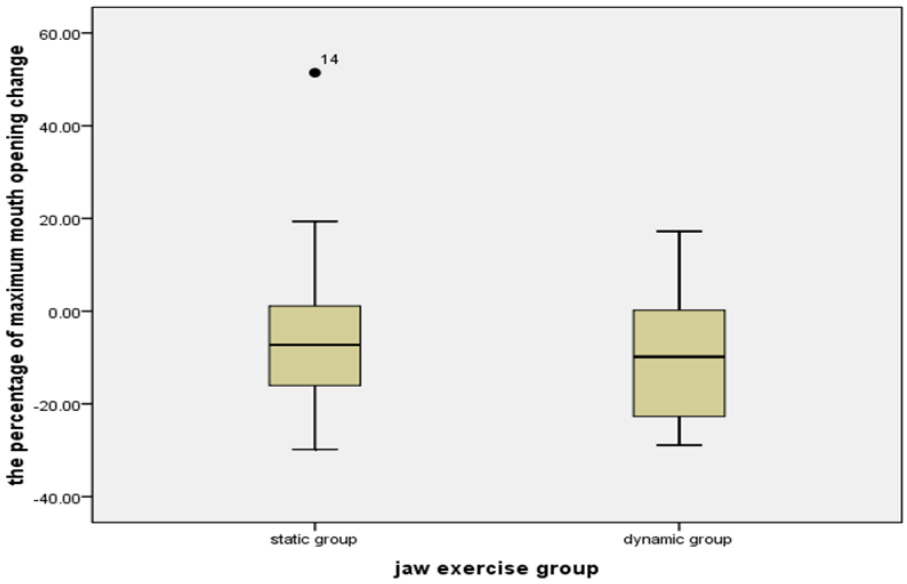


Figure 26 Demonstrate the percentage change of the maximum mouth opening distance of the static and dynamic jaw exercise groups

Table 5 Demonstrate the average percentage change of the maximum mouth opening distance excluded outlier

Group	Number of patients	Average percentage of MMOD change at 6 months post-RT compared to Pre-RT	
		Mean (SD)	Range
Static	18	-7.66 (13.47)	(-)29.82 to (+)19.35
Dynamic	20	-9.58 (13.89)	(-)28.89 to (+)17.24

The average percentage of maximum mouth opening distance reduction at 6 months post-radiotherapy compared to pre-radiotherapy of 11 patients in the static group and 15 patients in the dynamic group who received 2DXRT technique were 12.88% and 10.62% respectively. There was no significant difference between both groups (p = 0.668). For the patients who received IMRT technique from static (8 patients) and dynamic (5 patients) groups, their average percentage of maximum mouth opening distance change were 6.91% increase and 6.45% decrease respectively which were not significant different (p = 0.247). **(Table 6)**

Table 6 Demonstrate the average percentage of maximum mouth opening distance change between static and dynamic technique classified by RT technique

Radiation type	Group (n)	Percentage of MMOD change between pre-RT and 6 months post-RT	P-value
2DXRT	Static (11)	(-)12.88	0.668
	Dynamic (15)	(-)10.62	
IMRT	Static (8)	(+)6.91	0.247
	Dynamic (5)	(-)6.45	

In the other way, analysis of the average percentage of maximum mouth opening distance change between the patients who received 2DXRT and IMRT technique of the static group at 6 months post-radiotherapy compared to pre-radiotherapy, there was significant difference between both groups (p = 0.019)

(Table 7) even though the outlier was excluded (p = 0.034) **(Table 8)**. Contrary to those of dynamic group, there was no significant difference between 2DXRT and IMRT groups (p = 0.575). **(Table 7)**

Table 7 Demonstrate the average percentage of maximum mouth opening distance change between IMRT and 2DXRT technique of both groups

Group	Radiation type (n)	Average percentage of MMOD change between pre-RT and 6 months post-RT	P-value
Static	2DXRT (11)	(-)12.88	0.019*
	IMRT (8)	(+)6.91	
Dynamic	2DXRT (15)	(-)10.62	0.575
	IMRT (5)	(-)6.45	

Table 8 Demonstrate the average percentage of maximum mouth opening distance change between IMRT and 2DXRT technique of the static groups (outlier excluded)

Group	Radiation type (n)	Average percentage of MMOD change between pre-RT and 6 months post-RT	P-value
Static*	2DXRT (11)	(-)12.88	0.034*
	IMRT (7)	(+)0.55	

10 patients (25.64%) (5 from each group) had increased maximum mouth opening distance at 6 months after radiotherapy. They were diagnosed as tongue cancer (20%), parotid gland cancer (20%), nasopharyngeal carcinoma (40%), and base of tongue cancer (20%). 6 of them (60%) were treated with IMRT and the rest (40%) were treated with 2DXRT. 4 patients had trismus before radiation (maximum mouth opening distance ≤ 35 mm.). **(Table 9)**

Table 9 Demonstrate the data of the patients with increased maximum mouth opening distance at 6 months after radiation compared with pre-radiotherapy

No.	Tumor site	RT technique*	Pre-RT MMOD**	6 months post-RT MMOD***
S1	Tongue	IMRT	44	45
S22	Parotid gland	IMRT	35	40
S23	Parotid gland	IMRT	31	37
S32	Nasopharynx	IMRT	35	53
S35	Base of tongue	2DXRT	38	40
D15	Nasopharynx	IMRT	47	48
D34	Tongue	2DXRT	29	34
D35	Base of tongue	2DXRT	40	44
D36	Nasopharynx	IMRT	55	60
D37	Nasopharynx	2DXRT	53	55

S = Static group patients

D = Dynamic group patients

* RT technique = radiotherapy technique

(IMRT = Intensity-Modulated Radiation Therapy / 2DXRT = Conventional external beam radiotherapy)

** Pre-RT MMO = pre-radiotherapy maximum mouth opening distance (mm.)

*** 6 months post-RT MMO = 6 months post-radiotherapy maximum mouth opening distance (mm.)

From the questionnaires, the patients reported that jaw exercise did not cause any trouble (excessive pain) or disturb their daily lives (frequency and ease of use) although sometimes pain might negatively affect the exercise. Some of them felt inconvenient to do the jaw exercise with device (tongue blade stack and fingers) in public places but they still used the device in private places. The tongue blade sticks were generally available and no device needed for the finger-forced opening technique. Even they lost some degree of mouth opening distance, it did not affect

their daily life (speaking, eating, and oral hygiene maintenance). Overall both groups were satisfied with either jaw exercise technique they had.

Chapter 5
Discussion

Trismus is one of the most important complications related to head and neck radiotherapy. It was caused by the radiation induced fibrosis within the masticatory muscles, soft tissues of the cheek, or temporomandibular joint. Trismus was negative impact on the patient's quality of life. The incidence of trismus in irradiated head and neck cancer patients is high thus it is utmost important. Doctors and dentists who look after these patients should be aware of and try to prevent this complication. Unfortunately it was not paid attention enough. (5, 9, 36, 38)

The widely-used treatment for trismus is jaw exercise with the same principles similar to the weight training. During a workout, intense lifting or exercise causes the slightly damage of the muscles. The fibers of the connective tissues, the ligaments that connect bones to other bones, and the tendons that connect muscles to bones were torn which is called "microscopic tears". These tears fatigue the muscles and cause the delayed onset muscle soreness (DOMS) in the next day. With proper rest and sufficient nutrients the muscles are slowly rebuilt over the following days, but full repair can take a week or more. Ordinarily old tissue is discarded before new tissue is synthesized. The digestion of protein provides the raw material that can be used to synthesize new muscles. As a result the muscles recovered by increase size, strength and muscle capacity.(67)

This study showed that the average percentage of maximum mouth opening distance of the patients in the static group decreased less than those of the dynamic group but not statistically significant, possibly because jaw exercise with the tongue blade stack stretched the masticatory muscle continuously and the force from the tongue blade stack was greater than the force from the patients' own fingers since the force from the fingers was related with the patients' strength and their ability also intention to stretch their fingers. They would reduce the finger force when they felt uncomfortable, pain or fatigue on their fingers, muscles or joints. In addition most patients in this study were elderly. Their fingers were not strong enough to stretch the jaws as widely as the tongue blade stack so they performed the weaker

fingered-jaw exercise than the tongued blade stacked-jaw exercise. However the area to place the appliance of the static and dynamic jaw exercise techniques were different, described as the anterior area for the dynamic group and the posterior area for the static group. Because of the hardness of tongue blade stack so it should be placed at the posterior area which was stronger than the anterior area in order to reduce the risk of tooth trauma or soft tissue injury. Moreover to perform the jaw exercise by fingers at the anterior site was more convenient than at the posterior site. By the foregoing reasons, the position to place the static jaw appliance was at the posterior area and the dynamic one was at the anterior area. However, the difference of jaw stretching area not affect the stretching of the muscles as the patients of both groups were instructed to exercise by stretching their muscles as much as they could and the maximum mouth opening distance measurement was performed when the patients opened their mouth passively (without any assisting tools).

The study of Currivan et al. (1993) comparing the efficacy of three jaw exercise appliances : Therabite®, tongue blade stack, and finger-forced opening in the head and neck cancer patients with radiation induced trismus, revealed that the patients who used Therabite® had their maximum mouth opening distance increased more than the other two groups significantly. But there was no significant difference between the patients who used tongue blade stack and those with finger-forced opening. However, the patients in all three groups were advised to do the same jaw exercise technique which was dynamic jaw exercise, unlike this study that the patients in each group were assigned to do different jaw exercise techniques. The Therabite® is the jaw exercise appliance designed to move the mandible in accordance with the natural mandibular movement pathway and the clinician can define the range of its movement for the best therapeutic result. Because the opening force is under controlled by the patient, it increases the patient's compliance.(66) Unfortunately it is quite expensive and not available in Thailand, so it is not extensively used in Thailand. That was the reason why the patients in this study were advised to use the tongue blade stack as a static jaw exercise device or the fingers as a dynamic jaw exercise device.

From the total 66 patients, there were 27 patients excluded from the study by the reason of non-compliance (6), refusal to the radiotherapy (11), self-withdrawal from the study (2), change of the treatment plan to surgery due to the metastasis of the cancer to the larynx (1), and death from cancer during the study (7). Most of them refused the radiotherapy since they suffered from the pain caused by radiation induced mucositis and the complication of the radiation treatment. 2 patients left the study because they did not want to have the jaw exercise rehabilitation. It could be said that they did not perceive the effect and the advantage of jaw exercise so they were not aware of its importance. Six of them were not compliant with the exercise protocol, initially on account of the pain related to mucositis, the agony from the disease and its treatment, also the indifference of them, and afterwards the understanding that the maximum mouth opening distance would be stable after finishing the radiotherapy course. It corresponded to the previous study which mentioned that the strongest influenced factors to the patient's compliance with Therabite® were the internal motivation and the perceiving of the jaw exercise benefit. Initially, the cooperation was encouraged by the internal motivation, afterwards the perceiving of the jaw exercise effect would sustain the internal motivation, and later reaching their goal of mouth opening or understanding of no further maximum mouth opening distance reduction would make the patients decrease or stop their jaw exercise. The reasons why the patients disliked the jaw exercise were its strangeness and annoyance including the daily practice requirement. Some of them stopped practicing during the exercise course because they thought it went well or forgot to practice. Pain related to radiation induced mucositis, nausea, and fatigue were also major negative influenced factor that involve the internal motivation. Besides some of them were inconvenient and embarrassed to do the jaw exercise with fingers or tongue blade stack both in private place and public area so they exercised without any devices. Thus the principal role of the dentist is to elucidate the patients about the importance of jaw exercise, encourage them to exercise, and manage their complications.(68, 69)

The average maximum mouth opening distance of most patients started to decrease after the 2nd week during radiation treatment since mucositis would appear

within the 3rd week of the radiation period and worsened as the more dose received. This caused soreness when they open their mouth widely then their maximum mouth opening distance reduced.(36, 38) There was weak inverse correlation between maximum mouth opening distance and jaw pain according to the study of Lindblom et al. (2014).(70) One month post-radiotherapy the mucositis alleviated thus their maximum mouth opening distance began to increase but still less than those at the beginning. Afterwards their maximum mouth opening distance started to decrease again due to the fibrosis of muscles and soft tissue associated with radiation. It was corresponded to the study of Chon-Jong Wang et al. (2005) which said that the maximum mouth opening distance of the irradiated nasopharyngeal carcinoma patients started to decrease within the first week of radiation and the rate was directly proportional to the time since radiation was administered and at 1st - 9th month post-radiotherapy, the rate of decrease mouth opening distance becomes rapid.(57)

There were only 4 patients (3 from static group and 1 from dynamic group) (10.26%) in this study received only radiotherapy. One of them had 5.26% increased maximum mouth opening distance after radiation treatment since he had limited mouth opening from tumor at the beginning (38 mm.). The other 3 patients had 1.75% (static group), 13.04% (static group), and 7.69% (dynamic group) decreased maximum mouth opening distance respectively. 2 of 3 had their maximum mouth opening distance decreased less than the average of their group and the other had his maximum mouth opening distance decreased more than the average of his group. Hence it showed that there was no association between chemotherapy and the change of maximum mouth opening distance in these patients. In the same way, the study of Louise et al. (2008) indicated that the incidence of trismus of patients who received only radiotherapy and of those who received both chemotherapy and radiotherapy was not different significantly.(46) Contrary to the study of Krasin et Al. (2012) which said that receiving chemotherapy adversely affected maximum mouth opening distance in the first 12 weeks from initiation of radiation.(53) However, in this study, it was the comparison of the maximum mouth opening change between pre-radiotherapy and 6 months post-radiotherapy so the complications due to

chemotherapy which were short-term complications, might alleviate. In addition, the patients who received only radiotherapy in this study were limited (4 patients) therefore it could not be concluded whether chemotherapy affected the maximum mouth opening distance of irradiated head and neck cancer patients.

8 of 19 patients (42.11%) from the static group (4 were diagnosed as nasopharyngeal carcinoma, 2 were parotid gland cancer, 1 was tonsil cancer, and the other was tongue cancer) treated with IMRT had 6.91% increased average maximum mouth opening distance while the other 11 patients (57.89%) treated with conventional external beam radiotherapy (2DXRT) decreased their maximum mouth opening distance by 12.88%. The average percentage of maximum mouth opening distance change of the patients in the static group who received IMRT was increased and significantly different from those who received 2DXRT which was decreased ($p = 0.019$). It was similar to the study of Bensadoun et al. (2010) which demonstrated that the trismus prevalence was 25.4% for patients who received 2DXRT and 5% for those who received IMRT(61). IMRT provides better target conformity and spare more normal tissue (more radiation dose to the tumor and less dose to the surrounding tissue), therefore the complications from IMRT are less than conventional technique.(15, 71)

In the dynamic group, 5 patients (25%) with nasopharyngeal carcinoma treated with IMRT had 6.45% decreased average maximum mouth opening distance while the other 15 patients (75%) treated with 2DXRT had 10.62% decreased. However the change between the IMRT group and the 2DXRT group was not statistically significant ($p = 0.575$). It was homogeneous with the study of Louise et al. (2008) showed that there was no difference between the trismus prevalence of the patients treated with 2DXRT and of those who received IMRT.(46) It was likely because of the proximity to the masticatory apparatus of the tumors so the normal oral tissue received the full dose of radiation. From this study it could not be concluded that IMRT could improve trismus compare to the conventional radiotherapy.

In this study 10 patients (25.64%) (5 from each group) had increased maximum mouth opening distance 6 months after radiotherapy. They were

diagnosed as tongue cancer (20%), parotid gland cancer (20%), nasopharyngeal carcinoma (40%), and base of tongue cancer (20%). 6 of them (60%) were treated with IMRT and the rests (40%) were treated with conventional external beam radiotherapy (2DXRT). 4 patients had trismus before radiation (maximum mouth opening distance ≤ 35 mm.). All of them claimed that before starting the cancer treatment, they had pain or there were something interrupted when they opened their mouth. The previous study revealed that the patients with carcinoma of tonsils, oropharynx, retromolar trigone, and parotid gland were more likely to have trismus as the side effects from the tumors.(60, 72) Moreover trismus is one of the signs of the nasophyngeal carcinoma.(27) It was possible that some of these patients had trismus from the tumors. When they received the radiation, the tumors shrank and relieved, along with regular jaw exercise. As a result they would open their mouth wider. However it was still ambiguous so the further study should be done.

At the last visit (6 months after radiation) the questionnaires about the difficulty of using the jaw exercise technique and the daily life disturbance due to the reduction of the maximum mouth opening distance were collected. The patients reported that jaw exercise did not cause troubles (excessive pain) or disturb their daily lives (frequency and ease of use) although sometimes pain might negatively affect the exercise. The tongue blade sticks were generally available and no device needed for the finger-forced opening technique. Some of them felt inconvenient to do the jaw exercise with device (tongue blade stack or fingers) in the public area but they still use the device in the private place. Even if their maximum mouth opening distance decreased, it did not affect their daily life (speaking, eating, and oral hygiene maintenance). It was possibly because most of the patients did not suffer severe trismus or could adapt themselves. Overall both groups were satisfied with either jaw exercise technique they had.

The limitations of this study were lack of a control group due to ethical problems and small sample size including the short follow-up period because of the limitation of time and the death of patients. The heterogeneity in patients' demographic aspects, tumors characteristic, and oncological treatment procedures were also other limitations. However this heterogeneity reflects clinical practice and

therefore enhances external validity. The patients' compliance was significant uncontrolled factors but the motivation and frequent follow-up could increase their cooperation.

Chapter 6
Conclusion

There were no significant effects on maximum mouth opening between dynamic (cross finger stretching) or static (tongue blade stack) jaw exercise technique in patients with radiotherapy of head and neck. Further study should be done with larger samples and longer follow up period for better result of the jaw exercise.

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APPENDIX

APPENDIX A

Research Subject Information sheet for all participants (in Thai)

Consent Form for All Participants (in Thai)

Questionnaire (in Thai)

เอกสารชี้แจงข้อมูลแก่ผู้เข้าร่วมโครงการวิจัย (Research Subject Information sheet)

ชื่อโครงการวิจัย

การเปรียบเทียบผลของการใช้เครื่องมือฝึกอ้าปากแบบพลวัตและแบบอพลวัตต่อระยะอ้าปากในผู้ป่วยโรคมะเร็งบริเวณศีรษะและคอที่ได้รับรังสีรักษา

วันที่ชี้แจง

ชื่อและสถานที่ทำงานของผู้วิจัย

ทพญ.จารุมนต์ ศิรประชา คณะทันตแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย

ชื่อผู้วิจัยร่วม

-

ผู้ให้ทุนวิจัย

ทุน 90 ปี จุฬาลงกรณ์มหาวิทยาลัย

ท่านได้รับการเชิญชวนให้เข้าร่วมในโครงการวิจัยนี้ แต่ก่อนที่ท่านจะตกลงใจเข้าร่วมหรือไม่ โปรดอ่านข้อความในเอกสารนี้ทั้งหมด เพื่อให้ทราบว่า เหตุใดท่านจึงได้รับเชิญให้เข้าร่วมในโครงการวิจัยนี้ โครงการวิจัยนี้ทำเพื่ออะไร หากท่านเข้าร่วมโครงการวิจัยนี้ท่านจะต้องทำอะไรบ้าง รวมทั้งข้อดีและข้อเสียที่อาจจะเกิดขึ้นในระหว่างการวิจัย

ในเอกสารนี้ อาจมีข้อความที่ท่านอ่านแล้วยังไม่เข้าใจ โปรดสอบถามผู้วิจัยหรือผู้ช่วยผู้วิจัยที่ทำโครงการนี้เพื่อให้อธิบายจนกว่าท่านจะเข้าใจ ท่านจะได้รับเอกสารนี้ ๑ ชุด กลับไปอ่านที่บ้านเพื่อปรึกษาหารือกับญาติพี่น้องเพื่อน หรือแพทย์ที่ท่านรู้จัก ให้ช่วยตัดสินใจว่าควรจะเข้าร่วมโครงการวิจัยนี้หรือไม่ การเข้าร่วมในโครงการวิจัยครั้งนี้จะต้องเป็นความสมัครใจของท่าน ไม่มีการบังคับหรือชักจูง ถึงแม้ท่านจะไม่เข้าร่วมในโครงการวิจัย ท่านก็จะได้รับการรักษาพยาบาลตามปกติ การไม่เข้าร่วมหรือถอนตัวจากโครงการวิจัยนี้ จะไม่มีผลกระทบต่อการได้รับบริการ การรักษาพยาบาลหรือผลประโยชน์ที่พึงจะได้รับของท่านแต่อย่างใด

โปรดอย่าลงลายมือชื่อของท่านในเอกสารนี้จนกว่าท่านจะแน่ใจว่ามีความประสงค์จะเข้าร่วมในโครงการวิจัยนี้ คำว่า “ท่าน” ในเอกสารนี้ หมายถึงผู้เข้าร่วมโครงการวิจัยในฐานะเป็นอาสาสมัครในโครงการวิจัยนี้ หากท่านเป็นผู้แทนโดยชอบธรรมตามกฎหมายของผู้ที่จะเข้าร่วมในโครงการวิจัยและลงนามแทนในเอกสารนี้ โปรดเข้าใจว่า “ท่าน” ในเอกสารนี้หมายถึงผู้เข้าร่วมในโครงการวิจัยเท่านั้น

โครงการวิจัยนี้มีที่มาอย่างไร และวัตถุประสงค์ของโครงการวิจัย

โรคมะเร็งบริเวณศีรษะและคอนี้จัดเป็นโรคมะเร็งที่พบได้บ่อยโดยองค์การอนามัยโลกได้ทำการสำรวจจำนวนผู้ป่วยโรคมะเร็งทั้งหมดในประเทศไทยในปี ๒๕๕๑ พบว่าผู้ป่วยที่เป็นโรคมะเร็งบริเวณศีรษะและคอจัดเป็นโรคมะเร็งที่พบมากที่สุดเป็นอันดับที่ ๖

วิธีการรักษาโรคมะเร็งบริเวณศีรษะและคอมีหลายวิธีด้วยกัน เช่น การผ่าตัด การฉายรังสีรักษา หรือการให้เคมีบำบัดโดยวิธีที่ใช้กันเป็นประจำคือการฉายรังสีรักษา แต่ทั้งนี้การรักษาโดยการฉายรังสีบริเวณศีรษะและคอ จะนำไปสู่การเกิดภาวะแทรกซ้อนหลายประการในช่องปาก ซึ่งหนึ่งใน

ภาวะแทรกซ้อนที่มีความสำคัญและอาจนำไปสู่การเกิดภาวะแทรกซ้อนอื่นๆตามมาได้คือภาวะขากรรไกรยึด ส่งผลให้ผู้ป่วยมีคุณภาพชีวิตภายหลังการรักษาโรคมะเร็งที่แย่ลง

ในปัจจุบันมีวิธีการและเครื่องมือที่ช่วยในการฝึกอ้าปากหลายชนิดด้วยกันโดยแบ่งประเภทของวิธีการออกเป็น ๒ ชนิดด้วยกัน ได้แก่ วิธีการฝึกอ้าปากแบบพลวัต (dynamic) และวิธีการฝึกอ้าปากแบบอพลวัต (static) แต่ยังไม่เคยมีงานวิจัยใดทำการเปรียบเทียบประสิทธิภาพในการฝึกอ้าปากระหว่างสองวิธีนี้ เพื่อป้องกันการเกิดภาวะขากรรไกรยึด ทั้งที่การป้องกันย่อมดีกว่าการรักษา

งานวิจัยนี้จึงทำขึ้นเพื่อเปรียบเทียบผลของเครื่องมือช่วยฝึกอ้าปากแบบพลวัต (dynamic) และแบบอพลวัต(static) ที่มีต่อระยะการอ้าปากที่ลดลงว่ามีความแตกต่างกันหรือไม่ อย่างไร โดยจะใช้ไม้ไอศกรีมเป็นตัวแทนของวิธีการแบบอพลวัต (static) และใช้การฝึกอ้าปากโดยใช้นิ้วมือช่วยเป็นตัวแทนของวิธีการแบบพลวัต (dynamic)

ท่านได้รับเชิญให้เข้าร่วมโครงการวิจัยนี้เพราะคุณสมบัติที่เหมาะสมดังต่อไปนี้

ผู้ป่วยโรคมะเร็งบริเวณศีรษะและคอที่ได้รับการรักษาโดยการฉายรังสีที่โรงพยาบาลมะเร็งชลบุรี โดยปริมาณรังสีที่ได้รับอยู่ในช่วง ๖๐ – ๗๐ Gy ในการแบ่งฉายรังสีขนาด ๑๘๐ – ๒๐๐ cGy ต่อวัน สัปดาห์ละ ๕ วัน

ท่านไม่สามารถเข้าร่วมโครงการวิจัยได้หากท่านมีคุณสมบัติดังต่อไปนี้

๑. ผู้ป่วยที่ไม่สามารถฝึกบริหารขากรรไกรตามที่กำหนดได้ เช่น ผู้ป่วยที่มีกล้ามเนื้อแขนอ่อนแรง ผู้ป่วยที่ไม่สามารถช่วยเหลือตัวเองได้ ผู้ป่วยที่มีความบกพร่องของระบบประสาท เป็นต้น
๒. ผู้ป่วยที่เคยได้รับรังสีรักษาบริเวณศีรษะและลำคอ
๓. ผู้ป่วยที่เคยได้รับการผ่าตัดในบริเวณที่เกี่ยวข้องกับกล้ามเนื้อในการอ้าปาก
๔. ผู้ป่วยที่มีโรคของข้อต่อขากรรไกร (Temporomandibular Disorder)
๕. ผู้ป่วยที่มีแผนการรักษาโดยการผ่าตัด
๖. ผู้ป่วยที่ไม่สามารถเข้าร่วมได้ตลอดการศึกษา
๗. ผู้ป่วยโรคมะเร็งที่เกี่ยวข้องกับกล้ามเนื้อบดเคี้ยว, ข้อต่อขากรรไกร หรือในบริเวณอื่นที่มีผลต่อการอ้าปาก
๘. ผู้ป่วยที่ไม่ให้ความร่วมมือ

กลุ่มตัวอย่างจะเก็บจากผู้ป่วยจากโรงพยาบาลมะเร็งชลบุรีทั้งหมดจำนวน ๔๐ ราย โดยแบ่งออกเป็น ๒ กลุ่มโดยการสุ่ม คือกลุ่มที่ใช้เครื่องมือแบบพลวัตและกลุ่มที่ใช้เครื่องมือแบบอพลวัตโดยผู้เข้าร่วมโครงการแต่ละรายจะต้องเข้าพบทันตแพทย์เพื่อทำการวัดระยะอ้าปากก่อนได้รับรังสีแสงแรก จากนั้นผู้เข้าร่วมโครงการจะได้รับคำแนะนำและอุปกรณ์ให้นำกลับไปบริหารขากรรไกรที่บ้าน และผู้เข้าร่วมจะได้รับการนัดให้มาติดตามผลและวัดระยะอ้าปากซ้ำทุก ๒ สัปดาห์ในระหว่างฉายรังสี (สัปดาห์ที่ ๒, ๔, ๖) และในวันสุดท้ายของการฉายรังสี หลังจากนั้นจะนัดผู้เข้าร่วมมาติดตามผลและวัดระยะอ้าปากในเดือนที่ ๑, ๓, และ ๖ หลังสิ้นสุดการฉายรังสี รวมจำนวนครั้งที่ผู้เข้าร่วมต้องเข้าพบทันตแพทย์ทั้งหมด ๘ ครั้ง

ท่านสามารถถอนตัวออกจากโครงการวิจัยหลังจากได้ลงนามเข้าร่วมโครงการวิจัยแล้วได้ทุกเมื่อ โดยสามารถแจ้งได้ที่ผู้วิจัย

ประโยชน์ที่คาดว่าจะได้รับจากโครงการวิจัย

๑. ได้แนวทางในการดูแล ป้องกัน บรรเทาและแก้ไข ภาวะขากรรไกรยึดจากการฉายรังสีบริเวณศีรษะและคอ
๒. ผู้ป่วยมีคุณภาพชีวิตและสภาวะช่องปากหลังฉายรังสีที่ดีขึ้น
๓. เป็นประโยชน์ต่อผู้ป่วยในการรับการรักษาทางทันตกรรม

ในกรณีมีข้อสงสัยหรือมีปัญหาเกิดขึ้นเกี่ยวกับโครงการวิจัยนี้ ผู้เข้าร่วมโครงการสามารถติดต่อผู้วิจัยได้ที่ ทพญ.จารุมนต์ ศิรประชา คณะทันตแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย เบอร์โทรศัพท์ ๐๘๙-๘๑๐-๖๘๔๗

หากท่านรู้สึกว่าได้รับการปฏิบัติอย่างไม่เป็นธรรมในระหว่างโครงการวิจัยนี้ ท่านอาจแจ้งเรื่องได้ที่คณะกรรมการพิจารณาการศึกษาวิจัยในคน โรงพยาบาลมะเร็งชลบุรี โทรศัพท์ ๐๓๘ – ๗๘๔๐๐๑ – ๕

ข้อมูลส่วนตัวของท่านที่ได้จากโครงการวิจัยครั้งนี้จะถูกนำไปใช้ในการนำเสนอข้อมูลที่ได้จากโครงการวิจัย เพื่อประโยชน์ทางวิชาการโดยไม่เปิดเผยชื่อนามสกุล ที่อยู่ของผู้เข้าร่วมในโครงการวิจัยเป็นรายบุคคล และมีมาตรการในการเก็บรักษาข้อมูลส่วนตัวและข้อมูลที่ได้จากโครงการวิจัยเป็นความลับ

หนังสือแสดงเจตนายินยอมเข้าร่วมการวิจัย (Informed Consent)
รับรองโดยคณะกรรมการพิจารณาการศึกษาวิจัยในคน โรงพยาบาลมะเร็งชลบุรี

ข้าพเจ้า (นาย, นาง, นางสาว).....

ได้รับทราบโครงการวิจัยเรื่อง "**การเปรียบเทียบผลของการใช้เครื่องมือฝึกอ้าปากแบบพลวัตและแบบอพลวัตต่อระยะอ้าปากในผู้ป่วยโรคมะเร็งบริเวณศีรษะและคอที่ได้รับรังสีรักษา**"

วันที่ลงนาม ...../...../.....

ก่อนที่จะลงนามในใบยินยอมให้ทำการวิจัยนี้ ข้าพเจ้าได้รับการอธิบายจากผู้วิจัยถึงวัตถุประสงค์ของการวิจัยวิธีการวิจัย อันตราย หรืออาการที่อาจเกิดขึ้นจากการวิจัย หรือจากยาที่ใช้ รวมทั้งประโยชน์ที่คาดว่าจะเกิดขึ้นจากการวิจัยอย่างละเอียด และมีความเข้าใจดีแล้ว

ผู้วิจัยรับรองว่าจะตอบคำถามที่ข้าพเจ้าสงสัยด้วยความเต็มใจและไม่ปิดบังซ่อนเร้น จนข้าพเจ้าพอใจ

ข้าพเจ้าเข้าร่วมในโครงการวิจัยนี้ด้วยความสมัครใจ โดยปราศจากการบังคับหรือชักจูง

ข้าพเจ้ามีสิทธิที่จะบอกเลิกการเข้าร่วมในโครงการวิจัยเมื่อใดก็ได้ และการบอกเลิกนี้จะไม่มีผลต่อการรักษาพยาบาลที่ข้าพเจ้าจะพึงได้รับในปัจจุบันและในอนาคต

ผู้วิจัยรับรองว่าจะเก็บข้อมูลเกี่ยวกับตัวข้าพเจ้าเป็นความลับ และจะเปิดเผยเฉพาะในรูปของสรุปผลการวิจัยโดยไม่มีการระบุชื่อนามสกุลของข้าพเจ้า การเปิดเผยข้อมูลเกี่ยวกับตัวข้าพเจ้าต่อหน่วยงานต่าง ๆ ที่เกี่ยวข้อง จะกระทำด้วยเหตุผลทางวิชาการเท่านั้น

ผู้วิจัยรับรองว่าหากเกิดอันตรายใด ๆ จากการวิจัย ข้าพเจ้าจะได้รับการรักษาพยาบาลและได้รับค่าชดเชยตามที่ระบุในเอกสารชี้แจงข้อมูลแก่ผู้เข้าร่วมโครงการวิจัย

ข้าพเจ้าจะได้รับเอกสารชี้แจงและหนังสือยินยอมที่มีข้อความเดียวกันกับที่นักวิจัยเก็บไว้ เป็นส่วนตัวข้าพเจ้าเอง ๑ ชุด

ข้าพเจ้าได้อ่านข้อความข้างต้นแล้ว มีความเข้าใจดีทุกประการ และลงนามในใบยินยอมด้วยความเต็มใจ

ลงชื่อ.....ผู้เข้าร่วมโครงการวิจัย
(.....ชื่อ-นามสกุล ตัวบรรจง)
ลงชื่อ.....ผู้ดำเนินโครงการวิจัย
(.....ชื่อ-นามสกุล ตัวบรรจง)
ลงชื่อ.....พยาน
(.....ชื่อ-นามสกุล ตัวบรรจง)
ลงชื่อ.....พยาน
(..... ชื่อ-นามสกุล ตัวบรรจง)

วันที่_____.

Patient HN_____ref. No._____.

ชนิดของเครื่องมือ ☐ ไม้ไอศกรีม ☐ นิ้วมือ

Maximum mouth opening distance (MMOD)_____mm.

❖ **ความพึงพอใจในการบริหารขากรรไกร**

- ท่านคิดว่าความถี่ในการบริหารขากรรไกร(วันละ 5 ครั้ง)มีความเหมาะสมหรือไม่

☐ มาก ☐ ปานกลาง ☐ น้อย ☐ น้อยที่สุด

- การบริหารขากรรไกรก่อให้เกิดความเจ็บปวดหรือความไม่สบายหรือไม่

☐ มาก ☐ ปานกลาง ☐ น้อย ☐ น้อยที่สุด

- การบริหารขากรรไกรส่งผลกระทบต่อการใช้ชีวิตประจำวันของท่านหรือไม่

☐ มาก ☐ ปานกลาง ☐ น้อย ☐ น้อยที่สุด

- อุปกรณ์ที่ใช้ในการบริหารขากรรไกรสามารถหาซื้อได้สะดวกหรือไม่

☐ มาก ☐ ปานกลาง ☐ น้อย ☐ น้อยที่สุด

- ท่านมีความพึงพอใจในการวิธีการฝึกบริหารขากรรไกรที่ท่านได้รับการแนะนำหรือไม่

☐ มาก ☐ ปานกลาง ☐ น้อย ☐ น้อยที่สุด

❖ **ความพึงพอใจในการใช้ชีวิตประจำวันที่เกี่ยวข้องกับระยะอ้าปากในปัจจุบัน**

ท่านคิดว่าระยะอ้าปากที่ลดลงในปัจจุบันส่งผลต่อการใช้ชีวิตประจำในด้านเหล่านี้หรือไม่

กิจกรรม	มาก	ปานกลาง	น้อย	น้อยที่สุด
• การพูด				
• การรับประทานอาหาร				
• การทำความสะอาดช่องปาก				
• การใช้ชีวิตประจำวันโดยรวม				

❖ **ข้อเสนอแนะ**

.....

.....

.....

APPENDIX B

Statistic Output

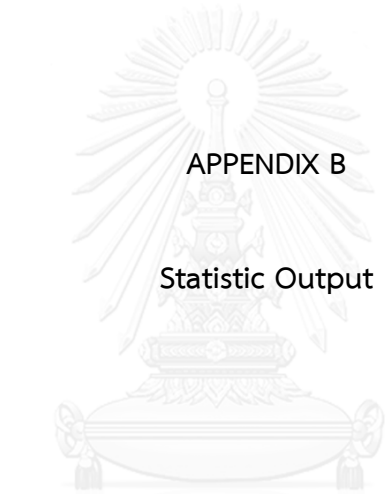

Table 1 Descriptive analysis and normality test of average percentage of maximum mouth opening distance change of both static and dynamic groups

One-Sample Kolmogorov-Smirnov Test

		the percentage of maximum mouth opening change
N		39
Normal Parameters[a,,b]	Mean	-7.1254
	Std. Deviation	16.46121
Most Extreme Differences	Absolute	.084
	Positive	.079
	Negative	-.084
Kolmogorov-Smirnov Z		.525
Asymp. Sig. (2-tailed)		.946

a. Test distribution is Normal.

b. Calculated from data.

Table 2 Demonstrate mean and standard deviation of average percentage of maximum mouth opening distance change of static and dynamic jaw exercise groups.

Group Statistics

	jaw exercise group	N	Mean	Std. Deviation	Std. Error Mean
the percentage of maximum mouth opening change	static group	19	-4.5458	18.83504	4.32105
	dynamic group	20	-9.5760	13.88812	3.10548

Table 3 Comparison of the average percentage of maximum mouth opening distance change between static and dynamic groups by Independent T-test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
the percentage of maximum mouth opening change	Equal variances assumed	.206	.653	.953	37	.347	5.03021	5.27996	-5.66801	15.72843
	Equal variances not assumed			.945	33.045	.351	5.03021	5.32123	-5.79536	15.85578

Table 4 and 5 Comparison of the average percentage of maximum mouth opening distance change between static and dynamic groups by Independent T-test (outlier excluded)

Group Statistics

	jaw exercise group	N	Mean	Std. Deviation	Std. Error Mean
the percentage of maximum mouth opening change	static group	18	-7.6556	13.45645	3.17172
	dynamic group	20	-9.5760	13.88812	3.10548

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
the percentage of maximum mouth opening change	Equal variances assumed	.278	.601	.432	36	.668	1.92044	4.44648	-7.09743	10.93832
	Equal variances not assumed			.433	35.789	.668	1.92044	4.43889	-7.08389	10.92478

Table 6 and 7 Comparison of the average percentage of maximum mouth opening distance change due to 2DXRT between static and dynamic technique

Group Statistics[a]

	jaw exercise technique	N	Mean	Std. Deviation	Std. Error Mean
percentage of maximum mouth opening change	static jaw exercise technique	11	-12.8764	11.36144	3.42560
	dynamic jaw exercise technique	15	-10.6173	14.24007	3.67677

a. type of radiation = 2D

Independent Samples Test[a]

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
percentage of maximum mouth opening change	Equal variances assumed	1.355	.256	-.434	24	.668	-2.25903	5.20715	-13.00607	8.48801
	Equal variances not assumed			-.450	23.775	.657	-2.25903	5.02528	-12.63590	8.11784

a. type of radiation = 2D

Table 8 and 9 Comparison of the average percentage of maximum mouth opening distance change due to IMRT between static and dynamic technique

Group Statistics[a]

	jaw exercise technique	N	Mean	Std. Deviation	Std. Error Mean
percentage of maximum mouth opening change	static jaw exercise technique	8	6.9087	21.65244	7.65529
	dynamic jaw exercise technique	5	-6.4520	13.79078	6.16742

a. type of radiation = IMRT

Independent Samples Test[a]

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
percentage of maximum mouth opening change	Equal variances assumed	.537	.479	1.223	11	.247	13.36075	10.92880	-10.69337	37.41487
	Equal variances not assumed			1.359	10.958	.201	13.36075	9.83060	-8.28649	35.00799

a. type of radiation = IMRT

Table 10 and 11 Comparison of the average percentage of maximum mouth opening distance change between IMRT and 2DXRT technique of the dynamic group

Group Statistics[a]

	type of radiation	N	Mean	Std. Deviation	Std. Error Mean
percentage of maximum mouth opening change	IMRT	5	-6.4520	13.79078	6.16742
	2D	15	-10.6173	14.24007	3.67677

a. jaw exercise technique = dynamic jaw exercise technique

Independent Samples Test[a]

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
percentage of maximum mouth opening change	Equal variances assumed	.009	.926	.570	18	.575	4.16533	7.30262	-11.17690	19.50757
	Equal variances not assumed			.580	7.093	.580	4.16533	7.18023	-12.76842	21.09909

a. jaw exercise technique = dynamic jaw exercise technique

Table 12 and 13 Comparison of the average percentage of maximum mouth opening distance change between IMRT and 2DXRT technique of static group

Group Statistics[a]

	type of radiation	N	Mean	Std. Deviation	Std. Error Mean
percentage of maximum mouth opening change	IMRT	8	6.9087	21.65244	7.65529
	2D	11	-12.8764	11.36144	3.42560

a. jaw exercise technique = static jaw exercise technique

Independent Samples Test[a]

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
percentage of maximum mouth opening change	Equal variances assumed	2.620	.124	2.596	17	.019	19.78511	7.62068	3.70689	35.86334
	Equal variances not assumed			2.359	9.809	.040	19.78511	8.38679	1.04867	38.52156

a. jaw exercise technique = static jaw exercise technique

Table 14 and 15 Comparison of the average percentage of maximum mouth opening distance change between IMRT and 2DXRT technique of static group (outlier excluded)

Group Statistics[a]

	type of radiation	N	Mean	Std. Deviation	Std. Error Mean
percentage of maximum mouth opening change	IMRT	7	.5486	13.01596	4.91957
	2D	11	-12.8764	11.36144	3.42560

a. jaw exercise technique = static jaw exercise technique

Independent Samples Test[a]

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
percentage of maximum mouth opening change	Equal variances assumed	.121	.733	2.312	16	.034	13.42494	5.80610	1.11656	25.73331
	Equal variances not assumed			2.239	11.594	.046	13.42494	5.99474	.31255	26.53732

a. jaw exercise technique = static jaw exercise technique

VITA

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