BAHAGIAN PENYELIDIKAN & PEMBANGUNAN
CANSELORI
UNIVERSITI SAINS MALAYSIA

RUJUKAN

Laporan Akhir Projek Penyelidikan Jangka Pendek

1) Nama Penyelidik: Dr Biswa Mohan Biswal.MBBS.MD.DNB

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3) Tajuk Projek: Topical application of honey in the management of radiation mucositis: A randomized trial.

4) (a) Penemuan Projek/Abstrak

(Perlu disediakan makluman di antara 100 - 200 perkataan di dalam Bahasa Malaysia dan Bahasa Inggeris Ini kemudiannya akan dimuatkan ke dalam Laporan Tahunan Bahagian Penyelidikan & Pembangunan sebagai satu cara untuk menyampaikan dapatan projek tuan/puan kepada pihak Universiti).

Radiation induced mucositis is a very common morbidity among head and neck cancer patients during radiotherapy. The intensity of mucositis varies according to different treatment parameters and can be reduced by physical and pharmacological intervention. This is a randomised trial to evaluate the efficacy of topical natural honey to prevent radiation mucositis. Forty diagnosed cancer patients requiring radiation to the head and neck area were randomised to receive radiation alone or radiation plus topical application of pure natural honey. Patients were treated using a 6-MV linear accelerator, at a dose rate of 2 Gy per day treating 5-times a week up to a dose of 60-70 Gy. In the study arm, patients were advised to take 20 millilitres of pure honey 15 minutes before, 15 minute after, and 6 hours post radiation therapy. Patients were evaluated every week for the development of radiation mucositis using RTOG grading system. The study was conducted between November 2000 and October 2001. There was significant reduction in the symptomatic grade 3/4 mucositis among honey treated patients compared to controls; i.e. 20% versus 75% (p 0.00058). The maximum intensity of mucositis was observed towards 3rd. weeks of radiotherapy on both arms. The compliance of honey treated group of patients was better than controls. Fifty five percent (55%) of patients treated with topical honey showed no change or positive gain of body weight compared to 25% in the control arm (p 0:053). In conclusion, topical application of natural honey is a simple and cost-effective treatment in radiation mucositis, which need further multi centre randomised trials to validate our finding.

Key words: radiation mucositis, acute morbidity, honey, and treatment

(b) Senaraikan Kata Kunci yang digunakan di dalam abstrak:

Bahasa Malaysia	Bahasa Inggeris
.....	Radiation mucositis
.....	acute morbidity
.....	honey
.....	treatment

5) Output Dan Faedah Projek

(a) Penerbitan *(termasuk laporan/kertas seminar)*
(Sila nyatakan jenis, tajuk, pengarang, tahun terbitan dan di mana ia telah diterbit/dibentangkan)

Preparing to present this paper in the coming 18th UICC International Cancer Congress, Oslo, Norway, 30th June-5th July 2002. Subsequently will be sent for publication.

(b) Faedah-Faedah Lain Seperti Perkembangan Produk, Prospek Komersialisasi Dan Pendaftaran Paten.
(Jika ada dan jika perlu, sila gunakan kertas berasingan)

As honey is a simple and cost effective product for the treatmentprevention and treatment of common problem radiation mucositis, it can be commercialise in the future. However it need further corroborative study to show that the result can be reproducible.

(c) Latihan Gunatenaga Manusia

i) Pelajar Siswazah .....

ii) Pelajar Prasiswazah: .....

iii) Lain-Lain : .....

6. Peralatan Yang Telah Dibeli:

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UNTUK KEGUNAAN JAWATANKUASA PENYELIDIKAN UNIVERSITI

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TANDATANGAN PENGERUSI
JAWATANKUASA PENYELIDIKAN
PUSAT PENYELIDIKAN

Topical application of honey in the management of radiation mucositis: A randomized trial.

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Under Short-term Research Grant
No 304/PPSP/6131132 (2000-2001)

Abstract

Radiation induced mucositis is a very common morbidity among head and neck cancer patients during radiotherapy. The intensity of mucositis varies according to different treatment parameters and can be reduced by physical and pharmacological intervention. This is a randomised trial to evaluate the efficacy of topical natural honey to prevent radiation mucositis. Forty diagnosed cancer patients requiring radiation to the head and neck area were randomised to receive radiation alone or radiation plus topical application of pure natural honey. Patients were treated using a 6-MV linear accelerator, at a dose rate of 2 Gy per day treating 5-times a week up to a dose of 60-70 Gy. In the study arm, patients were advised to take 20 millilitres of pure honey 15 minutes before, 15 minute after, and 6 hours post radiation therapy. Patients were evaluated every week for the development of radiation mucositis using RTOG grading system. The study was conducted between November 2000 and October 2001. There was significant reduction in the symptomatic grade-3/4 mucositis among honey treated patients compared to controls; i.e. 20% versus 75% (p 0.00058). The maximum intensity of mucositis was observed towards 3rd weeks of radiotherapy on both arms. The compliance of honey treated group of patients was better than controls. Fifty five percent (55%) of patients treated with topical honey showed no change or positive gain of body weight compared to 25% in the control arm (p 0.053). In conclusion, topical application of natural honey is a simple and cost-effective treatment in radiation mucositis, which need further multi centre randomised trials to validate our finding.

Key words: radiation mucositis, acute morbidity, honey, and treatment

Introduction

Management of head and neck cancer has undergone tremendous changes over the past 3-decades, with emphasis on organ preservation and multimodality management, including use of chemoirradiation. The latter approach is always associated with increased toxicity due to mucositis resulting in non-compliance to radiotherapy. About 500,000 newly diagnosed head and neck cancer cases are discovered worldwide[1]. Majority of these patients received chemotherapy, radiotherapy alone or in combination. However the degree of acute radiation morbidities depends upon the type and technique of chemotherapy and radiotherapy.

Radiation induced mucositis is an important complication of head and neck radiotherapy. Exposure of ionizing radiation to oral, pharyngeal and laryngeal mucosa gives rise to radiation epithelitis towards the 3rd week of conventional fractionated radiotherapy[2]. Severe radiation mucositis lead to ulceration and painful dysphagia that leads to poor quality of life and treatment discontinuation. The intensity of mucositis depends on the field size, interval between fractions, dose-per-fraction, previous exposure to chemotherapy, concurrent chemotherapy or co-

morbid medical conditions like diabetes mellitus or connective vascular disorders. The development of the oral mucositis is an inevitable accompaniment of radiation therapy to the head and neck region. The incidence of significant (grade 3 & 4) mucositis varies from 25 % to 50 % in various reported series [3-6]. There are various means to reduce incidence of radiation mucositis. The most common technique is to shield the unaffected mucosa by lead shields, use of conformation therapy, use of mouth bites, decreasing dose-per-fraction, and deliberate use of treatment breaks[7]. The above principles do not suit in certain circumstances like large tumour volume, and possibility of tumour resistance due to treatment gap.

The treatment of radiation-induced mucositis is not well established. However, many agents like topical sucralfate[8], subcutaneous or topical granulocyte macrophage colony stimulating factors (GM-CSF)[9-10], prostaglandin-E analogue misoprostol[11], topical corticosteroids[12], and parenteral radio-protector amifostine[13] have been tried with various response rates. Currently studies are on to find out newer agents, which are effective, safe and easy to use.

Honey is the concentrates of pollens from flowers collected by honey-bee. Though honey is an age-old remedy from the time of Egyptian civilisation, very recently it has found place in the modern medical

literature[14-15]. Honey has been found to be effective in burn wound, oral infections and healing of surgical wounds[16-18]. Honey has antibacterial properties and enhances epithelization thereby improve wound healing[19]. Researchers found a natural resin from honey, which are potent inhibitor of human colon adenocarcinoma cell growth, carcinogenic induction, biochemical changes and paraneoplastic lesion changes of rat colon[20]. Here we have used natural honey for the treatment of radiation mucositis to enhance epithelization of the mucosa, thereby reduce morbidity.

Materials and methods

Between November 2000 to October 2001, 40-patients undergoing radiotherapy to the head and neck region were randomised to receive either topical application of natural honey along with radiotherapy or radiotherapy alone. All the patient's treatment parameters were recorded in a special entry form. The quality-of-life (QoL) was measured before and after completion of radiotherapy using EORTC-QLQ-C30 (version 2.0) questionnaire. Patient's informed consent was obtained before starting radiotherapy.

Radiotherapy

Radiotherapy was administered using a 6-MV linear accelerator. The tumour volumes were assessed prior to simulation and adequate margins were taken depending upon the type of malignancy. Usually

parallel-opposed fields were used and tumour dose was calculated at the mid-plane. In multi-field technique, individual dose calculation technique was used. Conventional fractionated radiation was delivered to the tumour volume at a dose rate of 2-Gy per fraction, treating 5-fractions per week to a total period of 6-7 weeks. Individualised thermoplastic cast were made to treat tumours of the mobile parts of head and neck areas. External beam radiotherapy was delivered in three phases using shrinking field technique.

Assessment of the tumour response and development of complication was monitored every week on usual radiotherapy review clinic. Body weight recording and full blood count examination was performed on every assessment visit. Baseline liver function test, kidney function test, and blood sugar level were estimated before and after completion of radiotherapy. The development of mucositis was assessed using clinical and mirror examination of the mucosa. Radiotherapy and Oncology Group (RTOG) grading was utilised to grade the mucositis[21]. The treatment delays or gap are recorded in case of interval due to intolerable mucositis

Randomisation

Patients were randomised using the randomisation service of web site http://www.randomization.com. The patients were recruited as per the randomisation sequence for study and control arm patients. In the

treatment arm, pure natural honey was used. The patients were asked to take 20 ml of natural honey before radiotherapy, 20 ml after radiotherapy and 20 ml 6 hours there after. The patients were advised to rinse honey on the oral mucosa and then to swallow slowly to smear on the oral and pharyngeal mucosa. Both treatment and control arm patients were advised for adequate fluid intake and supplement high-protein diet.

Quality control of Honey

Honey used in this trial was obtained from the pure extracts of the beehives from the Malaysian rain forest. The above-obtained extract was filtered and supplied as raw or pure honey for the trial. The honey was subjected to chemical analysis and the pH was measured. A thin layer chromatography was used for the chemical analysis. The agent was extracted with potassium ether, chloroform, ethyl alcohol, methyl alcohol and developed to meet MeOH : H2O : CHCl3 proportion of 50:10:64. Vanilyn sulphuric acid test was done to find out glycoside compounds. Microbiological assay was done against pathogenic organisms at pure, 1:2, 1:4 and 1:8 dilutions respectively. Culture of *Pseudomonas auroginosa. Streptococcus pyogenes. Staphylococcus aureus, and Escherichia coli* were plated on agar plate. A filter disc was placed on the medium. About 30µl of the neat and 1:2, 1:4 and 1:8

diluted honey was placed on the disk. The medium was incubated for 18 hours and the inhibition zone was measured.

Response and toxicity criteria

The tumour regression was observed every week during radiation therapy and 8-weeks after completion of radiotherapy. The response measurement was done purely on clinical examination. Patients with complete regression of tumour was defined as complete response (CR), regression from 50% to 99% as partial response (PR), and less than 50% response as no response (NR). Development of oral and pharyngeal mucositis was grades as 0 for no change, 1 for mucosal erythema, 2 for studded mucositis, 3 for confluent mucositis not requiring intervention and 4 for ulceration, which necessitate treatment break as per the specifications of RTOG grading system[21].

Quality of life assessment

All patients were subjected to quality of life questionnaire as recommended by EORTC[22]. This is a questionnaire containing 43-questions related to the well being of the patients evaluated before and after completion of radiotherapy course.

Analysis

All the patients demographic and treatment related and morbidity scores were analysed using Microsoft-Excel software. The difference between the morbidities, nutritional parameters, treatment breaks and

total duration of mucositis etc was compared using Chi-square comparison from EPI info 2000 software.

Results

The study was completed in October 2001 and all the cases received radiotherapy as planned. The primary tumours were distributed in nasopharynx (9), larynx (7), paranasal sinuses (7), Thyroid (5) and other miscellaneous sites (12) (Table-1) The honey was subjected to microbiological assay to evaluate its antibacterial potency before administration to the patients. The honey showed good inhibition of bacterial growth proportionate to its concentration (Figure-1.a, b, c, d). Organisms like *Pseudomonas auroginosa, Escherichia coli, Streptococcus pyogenes and staphylococcus aurious* colonies showed good growth inhibition in vitro. Chemical analysis of the honey sample showed a pH of 4.8 and contains 5 compounds of terpinoids, tetraphenoids, trace elements, nitrogenous compounds, glycosides and sugars.

In the treatment arm, 16 patients showed some form of radiation mucositis, where as 19 patients in the control arm exhibited radiation

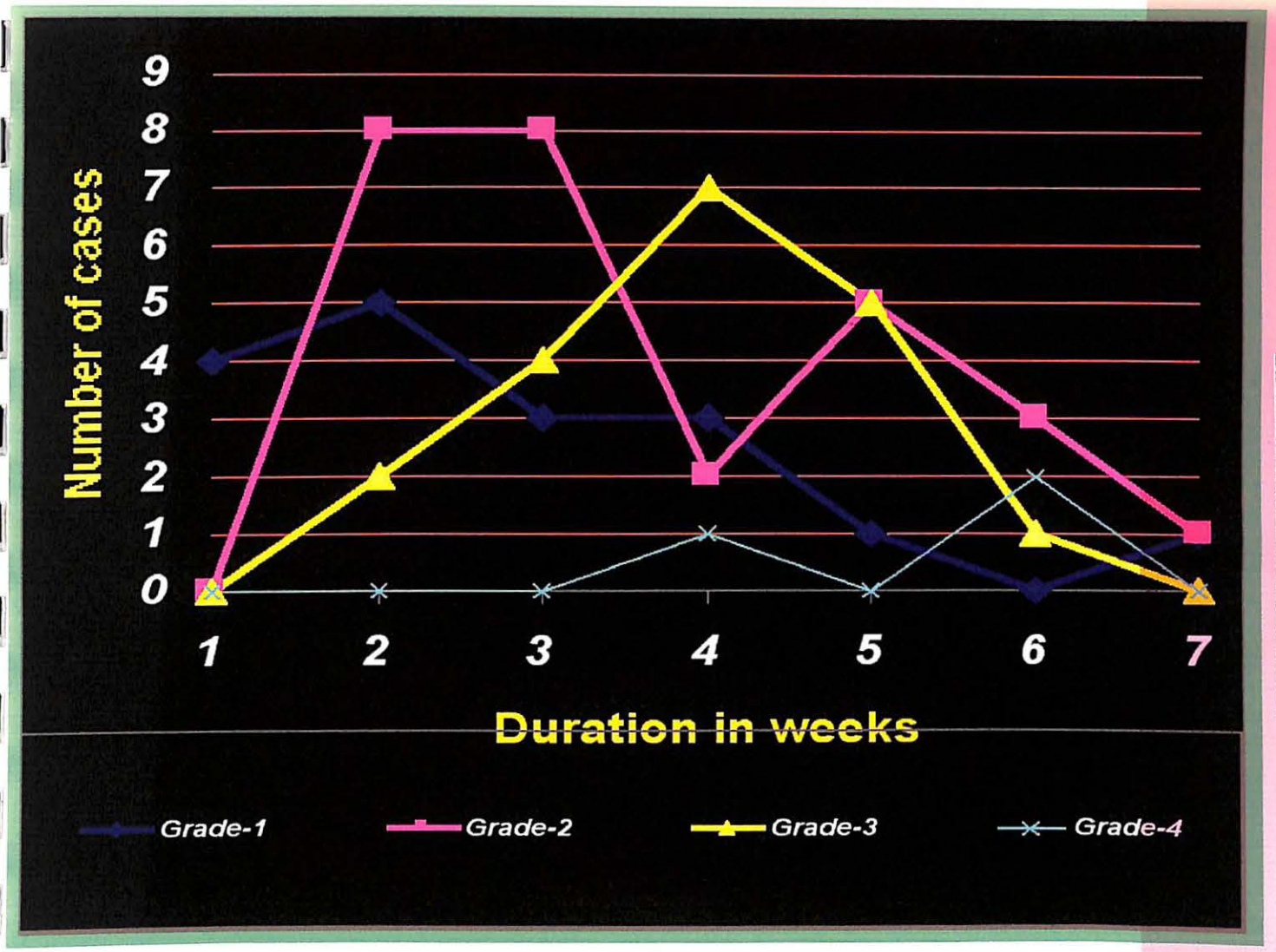


Fig - 2a CONTROL ARM

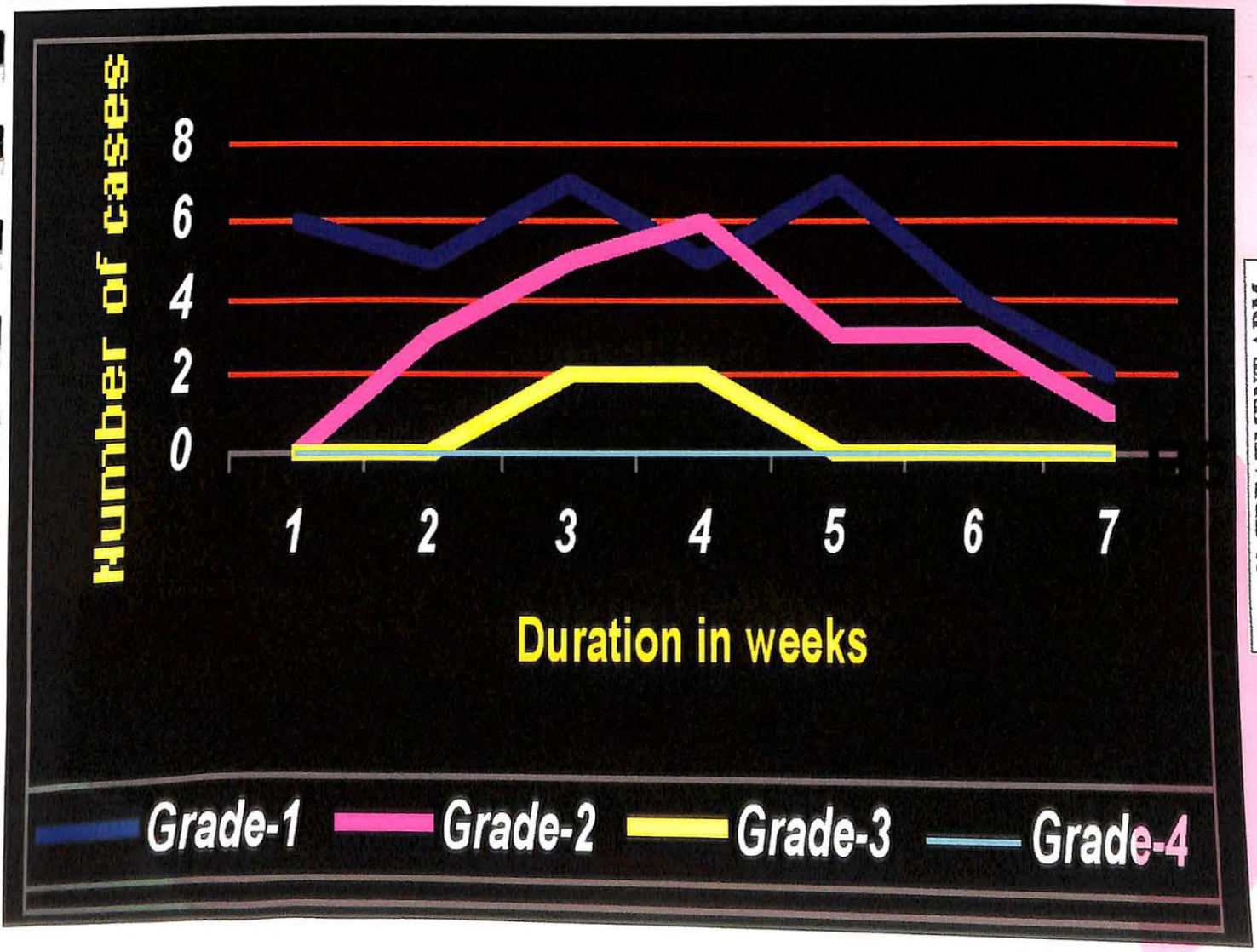


Fig - 2b TREATMENT ARM

Table-1.Patients characteristics

Total number of patients		40
Controls		20
Study arm		20
Male:Female Ratio		
Controls		8:12
Study arm		15:5
Age distribution (years)		
Controls		14 (minimum) 54 (median) 78 (maximum)
Treatment arm		19 (minimum) 63 (median) 89 (maximum)
Tumor location/ TNM classification		
T-category	Control	Study arm
T1	00	01
T2	01	01
T3	05	03
T4	12	12
N0	04	06
N1	06	03
N2	04	02
N3	03	04
M1	00	02
Location		
Nasopharynx	06	03
Larynx	01	06
Paranasal sinus	05	01
Thyroid	03	02
Miscellanenous sites	05	06
Mean radiation field size	132 cm2	153.4cm2

Table-2.Oral mucositis in honey-treated and control group of patients

Number of patients	20	20	NS
Patients with mucositis	16	19	NS
Patients with grade-3/4 mucositis	04	15	0.0005838
Mean grade of mucositis	3.05	3.3	NS
Mean onset of mucositis (week)	3	3	NS
Mean total duration of mucositis	07	07	NS
Negative body weight	09	11	NS
Static or positive body weight	11	05	0.0532299
Mean treatment breaks (days)	19.5	18	NS

Table-3.Distribution of mucositis during radiotherapy course

Controls	Week-1	Week-2	Week-3	Week-4	Week-5	Week-6	Week-7	Total
G0	16	05	04	07	09	11	16	68
G1	05	05	03	03	01	01	01	18
G2	01	08	08	02	05	03	02	29
G3	01	02	04	07	05	03	01	23
G4	00	00	01	01	00	02	00	04
Treatment								
G0	14	12	06	07	10	13	17	79
G1	06	05	07	05	07	04	02	36
G2	00	03	05	06	03	03	01	21
G3	00	00	02	02	00	00	00	04
G4	00	00	00	00	00	00	00	00

E. coli

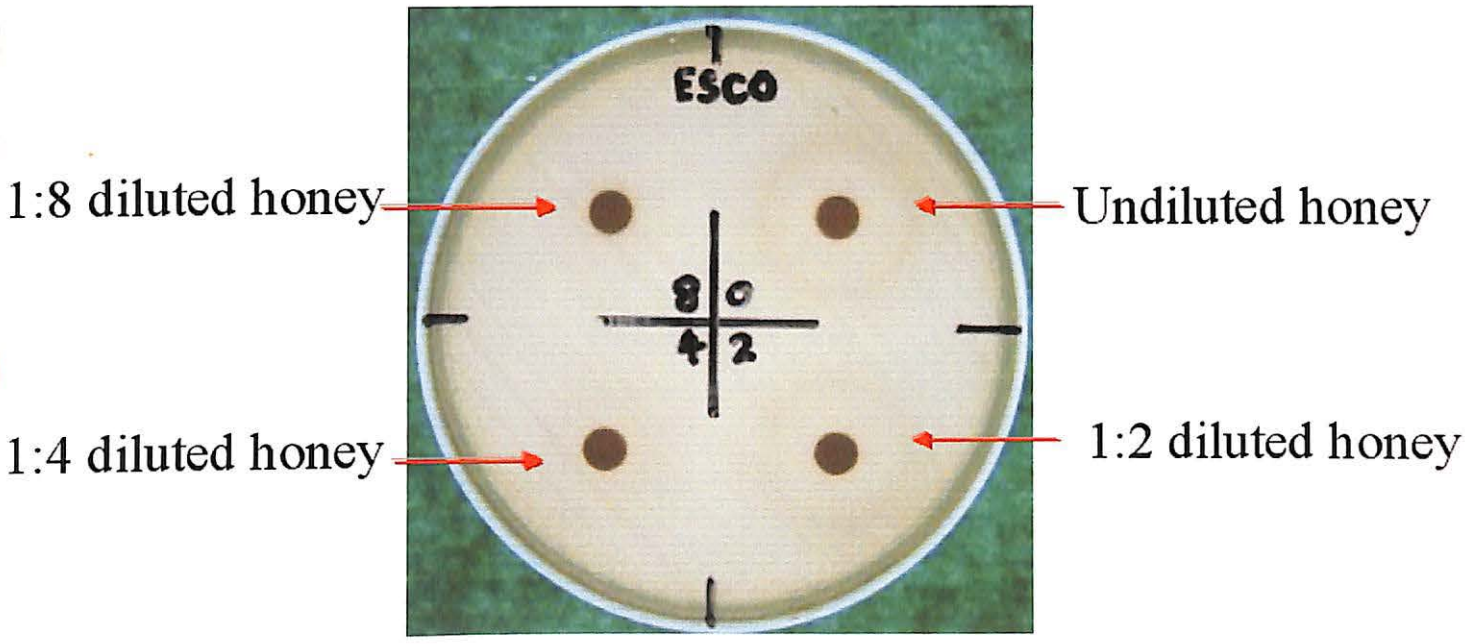


FIG - 1a

Pseudomonas aerugunosa

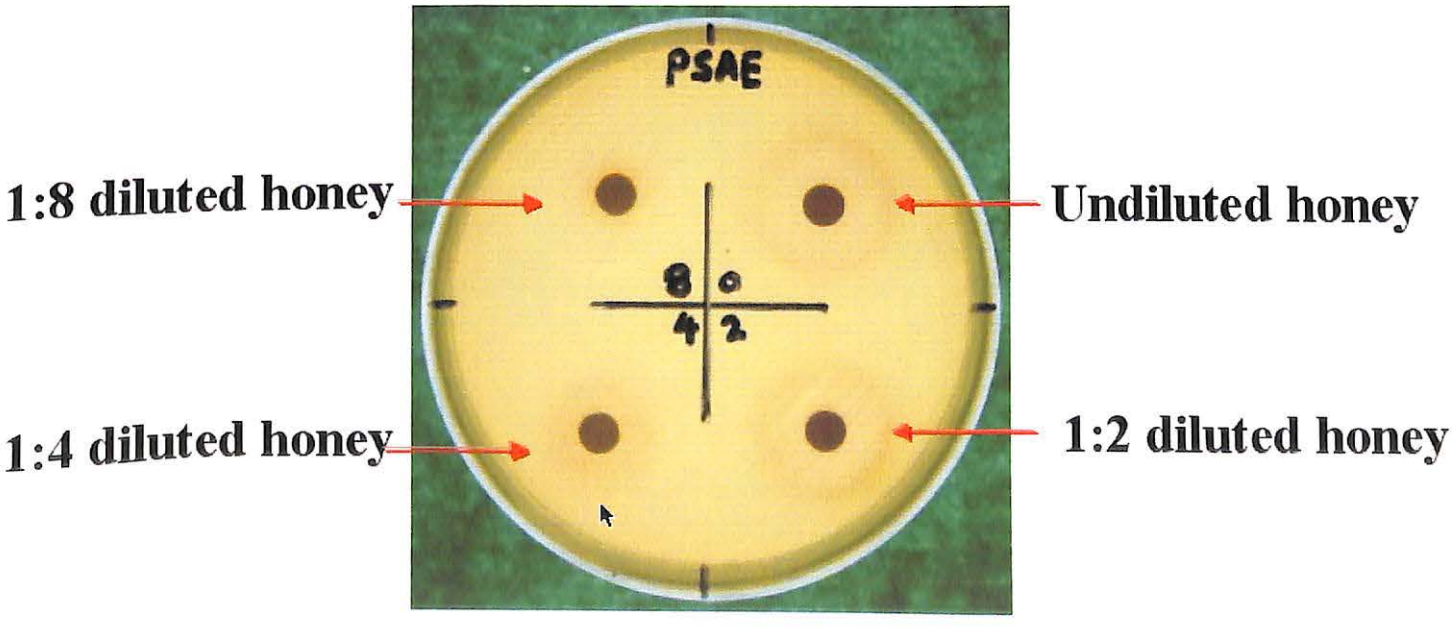
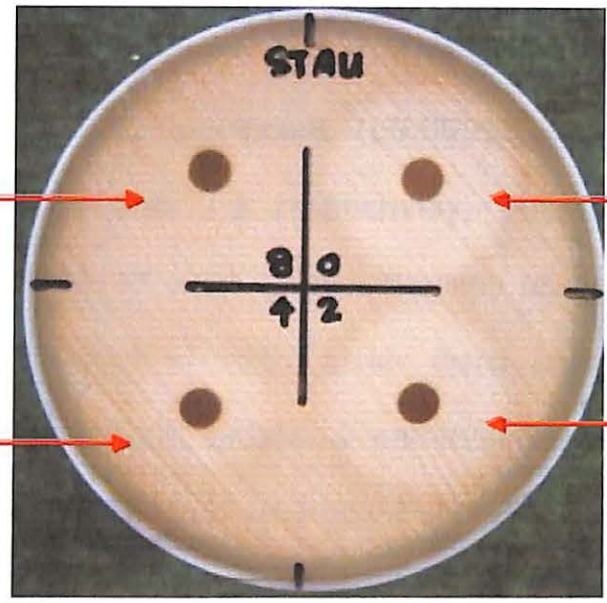


FIG - 1b

Staphylococcus aureus



1:8 diluted honey

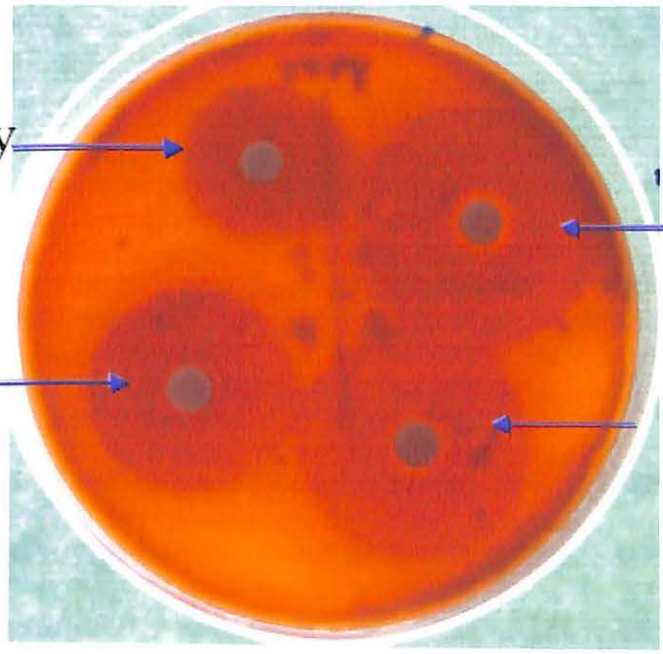
Undiluted honey

1:4 diluted honey

1:2 diluted honey

FIG - 1c

Streptococcus pyogenes



1:8 diluted honey

Undiluted honey

4 diluted honey

1:2 diluted honey

FIG - 1d

mucositis. The difference in the grade-3/4 mucositis was 20% and 75% respectively in the treatment and control arm (Table-2). The above finding was statistically significant (p0.00058). The mean grade of mucositis was 3.05 and 3.3 respectively, but the mean onset of mucositis was on the 3rd week of radiotherapy on both arms (Table-3). The treatment breaks in both arms were almost same. In the evaluation of weekly body weight, 9 patients from study arm and 11 patients from control arm showed some extent of loss of body weight. But interestingly 55% of the honey treated patients showed either static or positive gain in body weight during radiotherapy in comparison to 25% in the control arm. The difference in the patterns of mucositis in both arms is illustrated in figute-2a & 2b, which showed significant reduction in the grade-3 and grade-4 mucositis in the honey, treated group of patients.

Discussion

This study has shown encouraging results for the prevention of symptomatic radiation mucositis. Though there was no significant change in the grade-1 & 2 mucositis, but the grade-3/4 mucositis was significantly reduced in the treatment arm. At present there is no study on honey available to compare, however comparing to a prospective

randomised trial in the use of povidone iodine oral rinse, the results are similar[23]. But in our study we found an interesting observation regarding the change in body weight. In the study arm 55% of patients showed either static or gain in body weight during radiotherapy compared to 25% of patients on the control arm

Radiation induced mucositis is a normal accompaniment of radical radiotherapy to the head and neck area. Normally the oral mucosa has a relatively high cell turnover rate. Exposure to ionising radiation leads to mucosal erythema, small whitish patches, and ultimately results in confluent mucositis. In the later phases, oral ulceration and bleeding become a dose limiting toxicity. The mulcositis is a result of balance between cell loss and cell proliferation. The intensity of mucositis can be altered by new fractionation schedules, concurrent chemoradiotherapy, and co-morbid medical conditions. Bacterial colonization in the oral mucosa can exaggerate the mucositis. Endotoxins released from the gram-negative bacilli are potent mediator of the inflammatory process in the oral mucosa. Oropharyngeal flora too contribute to the radiation-induced mucositis[24-25]

Much has been reported about the mucositis and somatitis, but a lack of consistency and use of grading criteria and reporting standards

makes it very difficult to draw comparative conclusions concerning toxicity end points among various trials. The lack of standardization remains problematic, in spite of recent efforts to improve grading and reporting[2].

In 1981, the World Health Organization published grading criteria for 28 acute toxicities including mucositis[26]. Subsequently, National Cancer Institute's (NCI) common toxicity criteria in 1983, which included 49 chemotherapy related toxicity criteria scales along with mucositis[2]. On the next year an acute radiation toxicity system was published by Radiotherapy Treatment Oncology Group (RTOG)[21], followed by different toxicity criteria from the Eastern Cooperative Oncology Group (ECOG) and the South-West Oncology Group (SWOG). The latter two groups were basically used for chemotherapy-induced toxicities. Hence RTOG is one of the common toxicity scoring system to quantify radiation-induced mucositis.

The basis of management of radiation mucositis is targeted to its 4-defined pathogenesis. The most important of all is to check growth of basal cell layer by modifying transforming growth factor-β3 [27]. The second mechanism is by the rapid recovery of epithelial cell loss by the stimulation of epithelization [28-29]. Thirdly, by the chemical protection of

mucosa using aminothiol group of compounds like amifostine[30]. The last but not the least, physical method of preventing radiation exposure to the oral mucosa by the use of shield, conformation therapy or intensity modulated radiotherapy[31]. Local antibiotics in the form of lozenges have been tried with a hope to prevent bacterial colonization and reduce inflammation on the damaged mucosa. Low energy He/Ni laser treatment may promote the proliferation of mucosal cells and wound healing has been tried for the treatment of chemotherapy/radiotherapy-induced mucositis[32]. The above treatments are cumbersome and did not produce consistent results.

Honey is a pure natural extract of pollens from the wild flowers gathered by the honeybee. There is 4-types honey available for study i.e. sunflower, acacia, floral and wild floral type[33]. It contains moisture, fructose, glucose, sucrose, maltose and other compounds along with trace elements[34]. The quality of honey is basically depends upon the type of source and dilution. Pure honey is ubiquitous, cheap and natural, exhibit antibacterial, analgesic, and tissue nutritive factors to stimulate re-epithelization in the damaged mucosa, thereby a justified agent to try in radiation mucositis. Coating a wound with honey retard

tissue oxygenation by sealing the damaged mucosa off from air (oxygen). This could dampen pain within 30 seconds after application.

In the recent past, honey has been used for the treatment of burn wound, surgical infected wound, childhood diarrhoea, eye infections etc[15, 35]. The philosophy of using honey in radiation mucositis was derived from the basic research and clinical observation of rapid epithelization in tissue injuries[36-37]. In an experimental study by Bergman and co-workers, unboiled topical honey was applied to the open wound and the histopathological response was documented sequentially. The wound of the honey treated animals healed much faster than the wound of control animals (p value 0.001). According to this study, unboiled honey seems to accelerate wound healing when applied topically due to its energy producing properties, its hygroscopic effect on the wound, and its bacteriostatic properties. The important factors which influences the effectiveness of honey are

1.The hygroscopic nature of honey

2.Acidic pH of honey prevent bacteria to grow when applied to the mucosa

3.Inhibine (aka hydrogen peroxide) converted from glucose oxydase and gluconic acid

4.Enzymes (growth factors?) and tissue nutritive minerals and vitamins of honey help repair tissue directly.

Bacterial growth in the oral cavity can aggravate the effect of radiation mucositis. Study conducted by Al-Tikriti et al demonstrated that oropharyngeal flora contribute to radiation induced mucositis[24]. Endotoxins released by gram-negative bacilli are potent mediators of an inflammatory process[25]. Use of topical antibiotics like benzydamine has shown slight improvement in the control of mucositis. Another study by Rhan et al used povidone-iodine oral rinse to reduce chemo-radiotherapy induced mucositis. In their small randomised-trial, the severity and duration mucositis was reduced compared to controls treated with placebo (70% versus 100%) [23]. The antibacterial property of honey depends upon its concentration[38]. In our study we found bacterial growth inhibition around the honey drop, but the inhibition of the bacterial growth is inversely related to its dilution (figure-1a-d). Hence the reduction of radiation mucositis in honey treated patients might be due to bacteriostatic effect of viscid honey. The same osmolarity based bacteriostasis was demonstrated in other studies[39-40]. Pure honey is acidic with a pH of around 3.9 and the solubility-reducing factor present in honey can activate in absence of saliva. Honey applied on radiation induced xerotic mucosa increases the microhardness of enamel, there by prevent caries. Hence it has been postulated that honey is less cariogenic in dry mouth patients [41]. In a recently

published report from Russian Academy of Medical Science, patients treated with honey laminolact in uterine cancer patients on radiotherapy showed significant decrease in the severity of radiation induced intestinal morbidity[42].

In conclusion, from our small-randomised study, we found usefulness of pure natural honey in the management of symptomatic radiation mucositis. As this agent is effective in radiation mucositis, the same treatment could be useful in the management of chemotherapy induced oral stomatitis/mucositis and in the mucositis of bone marrow transplant patients. The philosophy of management in above conditions is similar. The further issue of use of medicinal honey need quality assurance of the natural honey, which might be different in different geographic locations, and source of pollens. As the future multimodality approach of cancer lies in chemo-radiotherapy and altered fractionation schemes, prevention of oral mucositis is very important in their management. Honey could be a simple and cheap agent for the management of above morbidity. However, further randomised studies are essential to validate our findings.

Acknowledgements:

This research was sponsored by short-term research grant (Grant No 304/PPSP/6131132) of Universiti Sains Malaysia, Malaysia. All the authors would like to thank Dr M. Ravichandran of Department of Microbiology, Mr Md Lukmi Ismail of department of Pharacology and Cik Ashikin for their help to carry out this project

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EORTC QLQ-C30 (version 2.0.)

We are interested in some things about you and your health. Please answer all of the questions yourself by circling the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

Please fill in your inititals: ____

Your birthdate (Day, Month, Year): ____

Today's date (Day, Month, Year): 31 ____

	No	Yes
1. Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2
2. Do you have any trouble taking a long walk?	1	2
3. Do you have any trouble taking a short walk outside of the house?	1	2
4. Do you have to stay in a bed or a chair for most of the day?	1	2
5. Do you need help with eating, dressing, washing yourself or using the toilet?	1	2

During the past week;	Not at All	A Little	Quite a Bit	Very Much
6. Were you limited in doing either your work or other daily activities?	1	2	3	4
7. Were you limited in pursuing your hobbies or other leisure time activities?	1	2	3	4
8. Were you short of breath?	1	2	3	4
9. Have you had pain?	1	2	3	4
10. Did you need to rest?	1	2	3	4
11. Have you had trouble sleeping?	1	2	3	4
12. Have you felt weak?	1	2	3	4
13. Have you lacked appetite?	1	2	3	4
14. Have you felt nauseated?	1	2	3	4
15. Have you vomited?	1	2	3	4

Please go on to the next page

During the past week:	Not at All	A Little	Quite a Bit	Very Much
16. Have you been constipated?	1	2	3	4
17. Have you had diarrhea?	1	2	3	4
18. Were you tired?	1	2	3	4
19. Did pain interfere with your daily activities?	1	2	3	4
20. Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	1	2	3	4
21. Did you feel tense?	1	2	3	4
22. Did you worry?	1	2	3	4
23. Did you feel irritable?	1	2	3	4
24. Did you feel depressed?	1	2	3	4
25. Have you had difficulty remembering things?	1	2	3	4
26. Has your physical condition or medical treatment interfered with your <u>family</u> life?	1	2	3	4
27. Has your physical condition or medical treatment interfered with your <u>social</u> activities?	1	2	3	4
28. Has your physical condition or medical treatment caused you financial difficulties?	1	2	3	4

For the following questions please circle the number between 1 and 7 that best applies to you

29. How would you rate your overall <u>health</u> during the past week?

1	2	3	4	5	6	7
Very poor						Excellent

30. How would you rate your overall <u>quality of life</u> during the past week?

1	2	3	4	5	6	7
Very poor						Excellent

EORTC QLQ-LC13

Patients sometimes report that they have the following symptoms. Please indicate the extent to which you have experienced these symptoms during the past week.

During the past week :	Not at All	A Little	Quite a Bit	Very Much
31. How much did you cough?	1	2	3	4
32. Did you cough blood?	1	2	3	4
33. Were you short of breath when you rested?	1	2	3	4
34. Were you short of breath when you walked?	1	2	3	4
35. Were you short of breath when you climbed stairs?	1	2	3	4
36. Have you had a sore mouth or tongue?	1	2	3	4
37. Have you had trouble swallowing?	1	2	3	4
38. Have you had tingling hands or feet?	1	2	3	4
39. Have you had hair loss?	1	2	3	4
40. Have you had pain in your chest?	1	2	3	4
41. Have you had pain in your arm or shoulder?	1	2	3	4
42. Have you had pain in other parts of your body?	1	2	3	4
If yes, where				
43. Did you take any medicine for pain?				
1 No 2 Yes				
If yes, how much did it help?	1	2	3	4

EORTC QLQ-C30 (version 2.0)

We are interested in some things about you and your health. Please answer all of the questions yourself by circling the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

Please fill in your initials: ☐☐☐☐

Your birthdate (Day, Month, Year): ☐☐ ☐☐ ☐☐

Today's date (Day, Month, Year): 31 ☐☐ ☐☐ ☐☐

		No	Yes
1.	Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2
2.	Do you have any trouble taking a <u>long</u> walk?	1	2
3.	Do you have any trouble taking a <u>short</u> walk outside of the house?	1	2
4.	Do you have to stay in a bed or a chair for most of the day?	1	2
5.	Do you need help with eating, dressing, washing yourself or using the toilet?,	1	2

	During the past week;	Not at All	A Little	Quite a Bit	Very Much
6.	Were you limited in doing either your work or other daily activities?	1	2	3	4
7.	Were you limited in pursuing your hobbies or other leisure time activities?	1	2	3	4
8.	Were you short of breath?	1	2	3	4
9.	Have you had pain?	1	2	3	4
10.	Did you need to rest?	1	2	3	4
11.	Have you had trouble sleeping?	1	2	3	4
12.	Have you felt weak?	1	2	3	4
13.	Have you lacked appetite?	1	2	3	4
14.	Have you felt nauseated?	1	2	3	4
15.	Have you vomited?	1	2	3	4

<u>Please go on to the next page</u>

During the past week:	Not at All	A Little	Quite a Bit	Very Much
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21. Did you feel tense?	1	2	3	4
22. Did you worry?	1	2	3	4
23. Did you feel irritable?	1	2	3	4
24. Did you feel depressed?	1	2	3	4
25. Have you had difficulty remembering things?	1	2	3	4
26. Has your physical condition or medical treatment interfered with your <u>family</u> life?	1	2	3	4
27. Has your physical condition or medical treatment interfered with your <u>social</u> activities?	1	2	3	4
28. Has your physical condition or medical treatment caused you financial difficulties?	1	2	3	4

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1	2	3	4	5	6	7
Very poor						Excellent

30. How would you rate your overall <u>quality of life</u> during the past week?

1	2	3	4	5	6	7
Very poor						Excellent

EORTC QLQ-LC13

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39. Have you had hair loss?	1	2	3	4
40. Have you had pain in your chest?	1	2	3	4
41. Have you had pain in your arm or shoulder?	1	2	3	4
42. Have you had pain in other parts of your body?	1	2	3	4
If yes, where				
43. Did you take any medicine for pain?				
1 No 2 Yes				
If yes, how much did it help?	1	2	3	4

RADIATION MUCOSITIS RESEARCH

Serial Number	**Treatment Arm A B**
Name	**HADS**
Age Gender Male/Female	**Race Malay/Chinese/Indian/Other**
IC Number	**QOL Score**
HUSM Number	**RT(Oncology) Number**
Date of first visit	**Date of last visit**

Diagnosis **TNM stage T N M**

ECOG performance status **0 , 1, 2, 3, 4**

Histopathology report with number and date

Aspiration cytology report and number and date

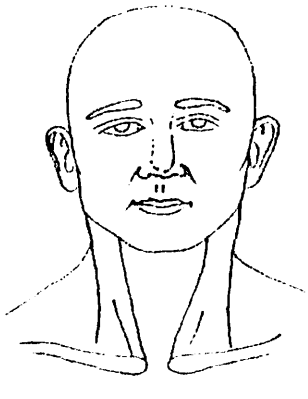
Prior medical illness Diabetes Hypertension Leucoplakia orodental problem others

Plan of treatment Radical Preoperative Postoperative Palliative Benign disease

Prior anticancer therapy Surgery Radiotherapy Chemotherapy Immunotherapy

Description of the tumor

Clinical **Nasoendoscopy/Laryngoscopy etc**



Radiotherapy details

Field design Parallel opposed 1-Field 2-Field 3-Filed Multi-field

Field Size in cm^2

Extent BOS-CLAV BOS-MIDNEK MANDIBLE-CLAV MAND-MIDNEK

Beam-modifying device shields wedges bolus compensator others

Radiation dose (in Gy) Phase-I Phase-II Phase-III

Fractionation scheme Gy Fractions Weeks

Duration of radiotherapy from to

Treatment intervals Yes No

Mucositis	Grade-I	Grade-II	Grade-III	Grade-IV	Grade-V
Week-1					
Week-2					
Week-3					
Week-4					
Week-5					
Week-6					
Week-7					
Week-8					

[Just put a cross sign (X) at the meeting point between week and grade of mucositis]

Other complications

Tumor response At end of radiotherapy 4-week post-RT 8-week post RT

RTOG Acute Radiation Morbidity Scoring Criteria

	[0]	[1]	[2]	[3]	[4]
SKIN	No change over baseline	Follicular, faint or dull erythema/ epilation/dry desquamation/ decreased sweating	Tender or bright erythema, patchy moist desquamation/ moderate edema	Confluent, moist desquamation other than skin folds, pitting edema	Ulceration, hemorrhage, necrosis
MUCOUS MEMBRANE	No change over baseline	Injection/ may experience mild pain not requiring analgesic	Patchy mucositis which may produce an inflammatory serosanguinitis discharge/ may experience moderate pain requiring analgesia	Confluent fibrinous mucositis/ may include severe pain requiring narcotic	Ulceration, hemorrhage or necrosis
EYE	No change	Mild conjunctivitis with or without scleral injection/ increased tearing	Moderate conjunctivitis with or without keratitis requiring steroids &/or antibiotics/ dry eye requiring artificial tears/ iritis with photophobia	Severe keratitis with corneal ulceration/ objective decrease in visual acuity or in visual fields/ acute glaucoma/ panopthalmitis	Loss of vision (unilateral or bilateral)
EAR	No change over baseline	Mild external otitis with erythema, pruritis, secondary to dry desquamation not requiring medication. Audiogram unchanged from baseline	Moderate external otitis requiring topical medication/ serious otitis medius/ hypoacusis on testing only	Severe external otitis with dischange or moist desquamation/ symptomatic hypoacusis/tinnitus, not drug related	Deafness
SALIVARY GLAND	No change over baseline	Mild mouth dryness/ slightly thickened saliva/ may have slightly altered taste such as metallic taste/ these changes not reflected in alteration in baseline feeding behavior, such as increased use of liquids with meals	Moderate to complete dryness/ thick, sticky saliva/ markedly altered taste	----	Acute salivary gland necrosis
PHARYNX & ESOPHAGUS	No change over baseline	Mild dysphagia or odynophagia/ may require topical anesthetic or non-narcotic analgesics/ may require soft diet	Moderate dysphagia or odynophagia/ may require narcotic analgesics/ may require puree or liquid diet	Severe dysphagia or odynophagia with dehydration or weight loss(>15% from pre-treatment baseline) requiring N-G feeding tube, I.V. fluids or hyperalimentation	Complete obstruction, ulceration, perforation, fistula
LARYNX	No change over baseline	Mild or intermittent hoarseness/cough not requiring antitussive/ erythema of mucosa	Persistent hoarseness but able to vocalize/ referred ear pain, sore throat, patchy fibrinous exudate or mild arytenoid edema not requiring narcotic/ cough requiring antitussive	Whispered speech, throat pain or referred ear pain requiring narcotic/ confluent fibrinous exudate, marked arytenoid edema	Marked dyspnea, stridor or hemoptysis with tracheostomy or intubation necessary

KEIZINAN DILAKUKAN TATACARA DAN RAWATAN RADIOTERAPI

Saya.....No. Kad Pengenalan .....

(nama)

beralamat .....dengan ini mengizinkan tatacara dan rawatan Radioterapi dilakukan keatas .....No. K/P : ..... untuk

(Saya/nama pesakit)

penyakit ..... yang mana sifat dan tujuannya telah diterangkan oleh Dr. ..... mengikut terjemahan ..... Beliau dengan sepenuh kemampuan dan kebolehannya telah menterjemahkan

(penterjemah)

kepada saya sifat dan kesan rawatan tersebut diatas dengan terang dan jelas dalam bahasa/loghat ..... tarikh ..... pertalian dengan pesakit..... *Tandatangan atau Cop Ibujari.....

(pesakit/waris)

DIHADAPAN

Nama : .....
No.K/P : ..... T/Tangan .....
Jawatan : .....
(Saksi)

Saya sahkan bahawa saya telah menerangkan kepada pesakit/waris, sifat dan kesan tatacara dan rawatan tersebut diatas.

Tarikh:..... Tandatangan:.....

(Doktor Yang Merawat)
Cop Rasmi

Keizinan mestilah ditandatangani oleh :-
(a) Ibubapa penjaga jika pesakit i dibawah umur
atau (b) Waris pesakit yang berumur tidak kurang dari 18 tahun jika pesakit itu tidak terdaya dari segi mental atau fizikal.

No.Pend.	
Nama	

JABATAN PERUBATAN NUKLEAR, RADIOTERAPI, & ONKOLOGI

Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan.

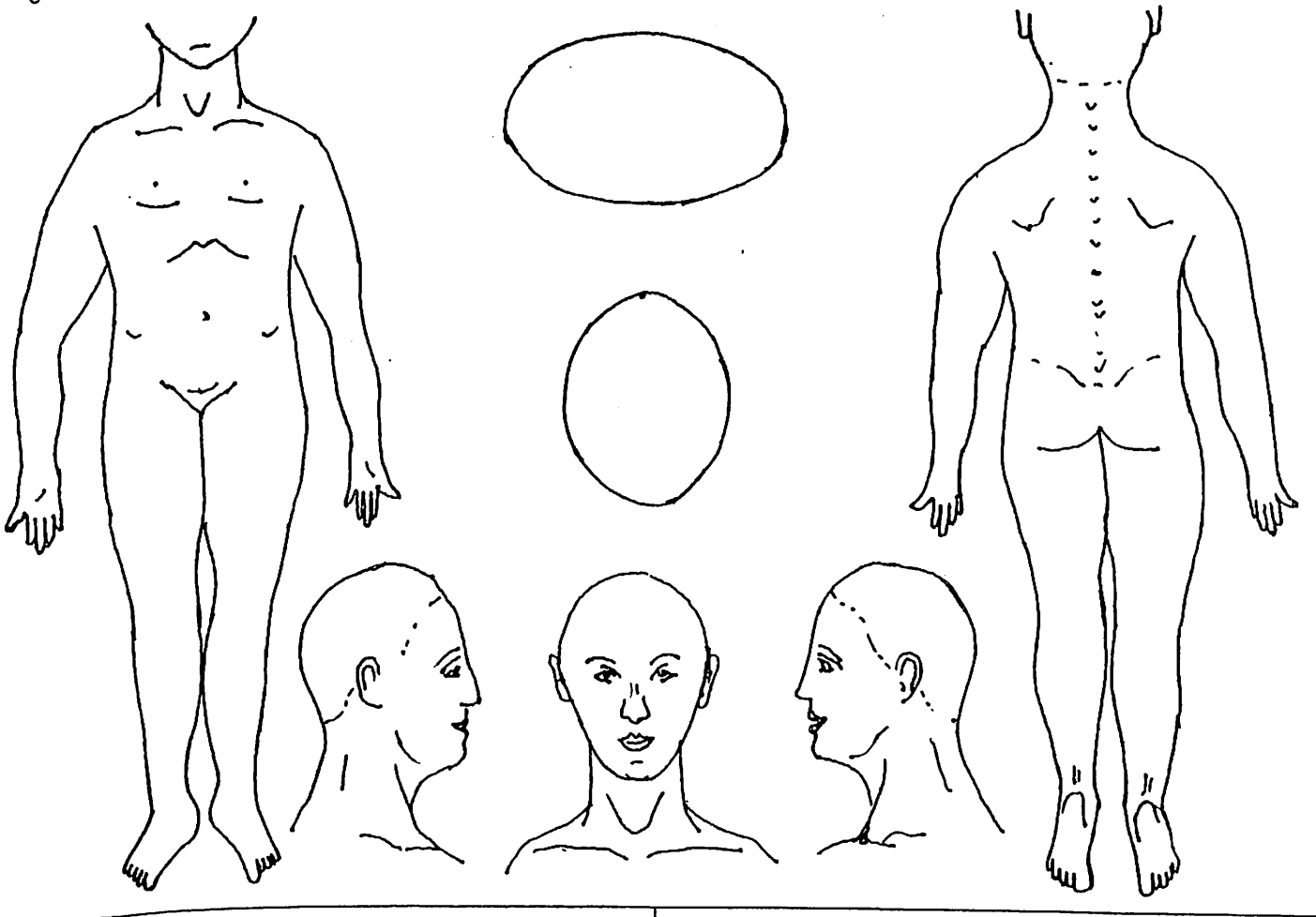
PATIENT DATA & RADIATION PRESCRIPTION

R	T						

NAME:	R/N:	OP/WARD:
ADDRESS:	SEX/AGE:	TEL. NO:
DIAGNOSIS:	CONSULTANT:	
INTENT : RADICAL / ADJ/PALLIATIVE / MISC.	**PROTOCOL : RT / Chem-RT / RT-Chem**	

DATE	SITE & TECHNIQUE	DOSE PRESCRIPTION	RADIATION TYPE & ENERGY	REPLAN & BOOST	REMARKS

Diagram : Original field, black; Modification, green; Reduction, red.



PRESCRIBED BY:	DATE:

TREATMENT SET-UP

FIELDS	NUMBER										
	NAME										
	JAWS										
	SIZE										
SSD / SAD (PIN)											
GANTRY ANGLE											
COLLIMATOR ROTATION											
COUCH ROTATION											
W'GE ANG. & DIRECTION											
SHIELDING / CUT OUT											
APPLICATOR											
BOLUS OR WAX											

PLANNING CALCULATION

FIELDS	Number						
	Size						
Eqv. Square @ SAD							
Treatment Machine							
Radiation / Energy							
Separation AP / Lat							
SAD/ SSD / Ext. SSD							
SSD / SAD Factor							
Sc @ depth							
Sp @ depth							
PDD / TMR @ depth							
Tray Factor							
Wedge Factor							
Weighting							
Tumor Dose (cGy)							
MU							
Calc. By							
Checked By							

DAILY DOSE CHART

FIELD		NO													
		SIZE													
TIME / M.U															
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