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天然抗菌P-113胜肽噴劑介入改善口腔癌病人接受化放療前後的口乾症狀及口腔黏膜炎與生活品質

The effects of P-113 peptide on improvement of xerostomia and oral mucositis to quality of life in oral cancer patients.

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Abstract

Background: Radiotherapy always cause some side effects, for example, xerostomia, mucositis, loss of taste, decayed tooth, hard to swallow. Radiation-induced toxicity can cause weakness, fatigue, decreased quality of life, an inability to tolerate treatment, and increased mortality.

Purposes: This study was to explore the effects of P-113 peptide on improvement of xerostomia and oral mucositis to quality of life in oral cancer patients.

Methods: A randomized controlled trial. Eighty participants were recruited and use the blocked randomization to assign them into the control group and the experimental group. The control group received routine care and the experimental gruop use the P-113.Data were collected at baseline, 3 weeks and 7 weeks after the intervention. The IBM SPSS 20.0 was to use to examine the effects with Generalized estimating equations.

Results: The results showed that the experimental group with Xerostomia significantly improved in the 7 weeks. ($p < .001$) However, no significant differences in improvement of oral mucositis between the control group and experimental group. The pain score of the experimental group after seven weeks was improved 11.67 points higher than the control group ($p = .003$)

Conclusion: P-113 can improve xerostomia and pain in oral cancer patients.

Keywords: head and neck cancer, radiochemotherapy, P-113 peptide, oral mucosa, quality of life

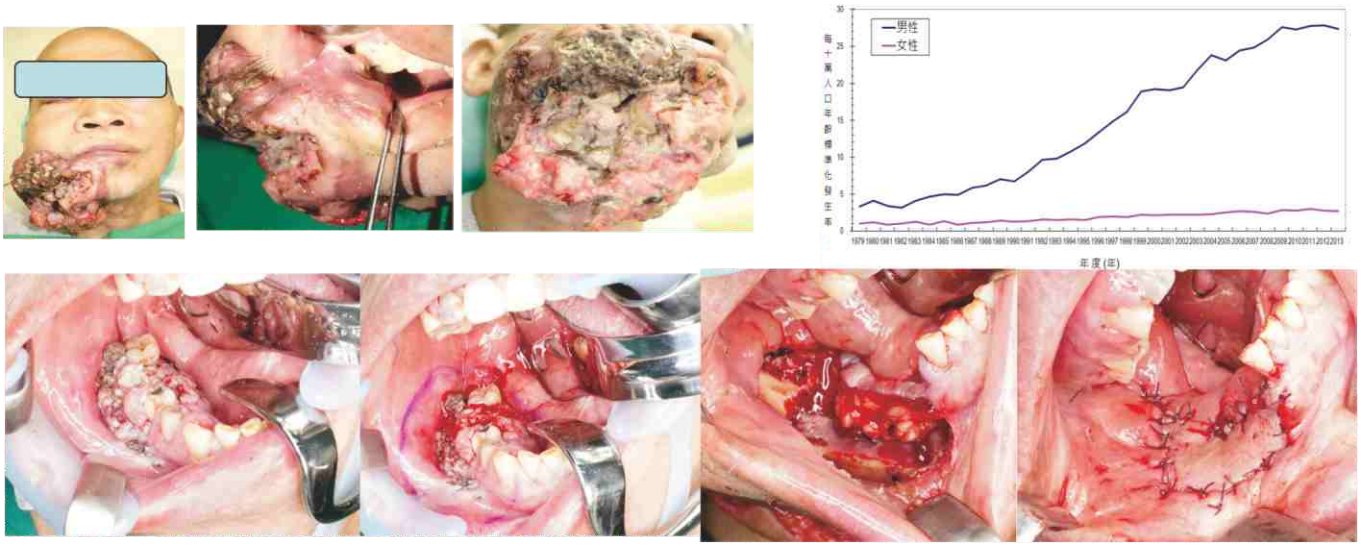
Introduction

口腔癌目前治療方式是以手術為主，在術後依照病理分期及相關危險因子來決定後續的放射線治療及化學治療，通常會進行大範圍的切除手術，一旦腫瘤及周遭組織被切除時，傷口重建決策也會隨之影響病人之吞嚥功能，而癌症分期越高，對吞嚥功能的影響也越大(相、

胡，2017)。吞嚥功能下降導致的吞嚥困難除了會造成脫水、營養不均衡或吸入性肺炎等生理問題(蔡、陳，2013)，營養是健康的基礎，一旦病人的營養狀況改變，身體無法吸收充分的營養時，則會降低抵抗力，進一步導致其他併發症及死亡的發生率提升(涂，2008)，而嚴重的吞嚥困難之病人則需要以鼻胃管灌食，但仍然有胃食道逆流及肺炎的危險，且病人無法與家人朋友一同進食，不但少了許多社交活動，也會對生活品質造成影響(賴、王、陳，2011)。口腔癌患者在接受不同的手術後，產生的副作用也不盡相同，而大部分的手術除了會改變患者的外表，同時也會影響其口腔的咀嚼功能，一旦咀嚼功能改變時，患者會變得十分困難甚至無法自行進食，可能導致其食慾降低，營養狀況也跟著改變。雖然在接受治療後，患者的壽命可以延長，但同時也可能造成其生理、心理、社會等層面的影響，除了疾病帶來的身體之不適，治療的過程同時也會造成患者的各層面之困擾，生活品質也隨之受到改變，因此不論是口腔癌或是手術及治療過程對患者來說，不但造成了身體之不適，更時時刻刻困擾著他們，其中常見的不適症狀有：味覺改變、口腔乾燥、患處疼痛、嘴巴潰瘍、喉嚨痛等，而這些症狀更嚴重降低患者進食的意願(Tomko et al., 2013)。從以上可以得知，口腔癌患者在術後除了需要面對自己的身體心像改變，也需要瞭解如何舒緩疾病及治療過程所帶來之不適，更需要家庭的支持及陪伴。

早期對於癌症病患的醫療較著重於患者壽命的延長，而現今則以提升患者的生活品質為目標，因此除了確認患者被哪些症狀所困擾著，也要緩解其症狀，同時瞭解患者的營養狀況，透過相關因素之探討，降低患者的症狀困擾，以提升患者進食之意願，進而改善其營養狀況，達到改善生活品質之目的。目前國內針對口腔癌患者的相關研究，較多提及症狀困擾與照護需求相關，較少探討患者經過放射線治療後的口乾症狀、口腔黏膜炎及其生活品質之影響，因此本研究欲透過早期介入，來改善口腔癌症因放射線或化學治療所引起的各種症狀，進而提升口腔癌病患的生活品質。

口腔癌為國人十大癌症排名中的第5名，更為男性排名中的第4名，台灣癌症登記中心統計分析國人口腔癌罹患率逐年上升，尤其在男性人口發生率由1979年3.28升高至2013年的27.41 (圖一)。



圖一、左上為惡性腫瘤第四期病人，右上為近期癌症發生比率線狀圖，下圖為惡性牙齦癌第四期手術切除及旋轉皮瓣修補術，口腔癌目前治療方式是以手術為主，後續放射線治療常導致病人卻步。

癌症治療引發之口腔黏膜炎意指因化學藥物治療或放射線治療後所引起的口腔黏膜紅斑、萎縮、發炎及潰瘍反應[1]。許多研究者針對癌症病人面對化學或放射線治療所引起的口腔黏膜炎進行研究，發現各種癌症病人面對不等程度之口腔黏膜衝擊，如Figliolia et al. (2008)追蹤169位急性淋巴性白血病接受化學藥物治療的患者，有46%（72位）患者發生口腔黏膜炎。根據陳、葉、莊、林（2003）調查152位首次接受化學藥物治療的癌症病人，在接受化學治療後35天內口腔黏膜炎發生率為31.5%，接受化療後每五天為一區間，結果顯示於化療後第5-10天發生口腔黏膜炎之機率9%，比其他區間發生口腔黏膜炎的機率還高。Vagliano et al. (2011)研究1579位接受高劑量化學治療後執行幹細胞移植的病人發生口腔黏膜炎之發生率，結果顯示口腔黏膜炎的時間長達10-14天，其中成年人(19-59歲)口腔黏膜炎發生率高達71%，其中有24.4%屬重度口腔黏膜炎，老年人(60-74歲)口腔黏膜炎發生率60.6%，其中有9.2%屬重度口腔黏膜炎。

口腔是一個特殊的人體生態環境，微生物菌叢與人體細胞保持平衡而能維持健康，唾液中的抗菌胜肽扮演很重要的角色。富組蛋白能夠抵抗細菌、真菌的感染，其中又以histatin 5具有最佳之抗菌作用，分析histatin 5中的不同組合片段，於全長24個胺基酸片段中又找出其中最短片段的12胺基酸，且具有最佳的抑菌作用之 P-113 胜肽，其序列為 AKRHHGYKRKFH-NH2 [13]。P-113 能阻礙白色念珠菌的單細胞體(yeast)和菌絲體(mycelium)兩種型態的菌株生長；亦具有多種細菌之抑菌作用，抗真菌的機制為與菌體接受器結合進入菌內。在粒線體呼吸氧化過程中，將所產生的能量以電化學位能儲存於粒線體內膜，此過程稱之為 mitochondrial membrane potential (DYm)，以此進行電子傳遞鏈產生ATP以供細胞使用，致使菌體粒線體腫脹、克氏循環(Krebs cycle)因malate dehydrogenase的負調控(down regulation)而被抑制，F1F0-ATPase complex表現下降而使得ATP產量降低，另外，elongation factor alpha 的表現上升而使得代謝不協調而最終電子傳遞鏈失去效用而使菌體死亡。

P-113 抗菌胜肽來源為口腔中耳下腺和頜下腺共同分泌之histatin 5(富組蛋白)，於唾液中具有抑菌效果，能夠抑制白色念珠菌、新型隱球菌(Cryptococcus neoformans)和煙麴黴(Aspergillus fumigatus)等真菌感染，維護口腔健康。P-113即為histatin 5中的12個胺基酸片段，是由多個組氨酸等陽離子所組成之抗菌胜肽，能抑制白色念珠菌的單細胞體(yeast)和菌絲體(mycelium) 兩種型態的生長；亦具有多種細菌之抑菌作用。

Materials & Methods

本研究主要針對口腔癌患者提供P-113胜肽噴劑介入方案，期望可以達到下列目的：

一、探討P-113胜肽噴劑介入方案於口腔癌患者的口乾症狀之成效。

二、探討P-113胜肽噴劑介入方案於口腔癌患者的口腔黏膜炎與生活品質之成效。

三、本研究為實驗性研究設計(Quasi-experimental design)，採立意取樣，以隨機分派至實驗組及控制組，採雙組前、後重複測量，採非平行式收集兩組資料，先進行實驗組收

案並接受P-113噴劑方案，待實驗組所有資料收集完成後，再進行控制組收案，並接受病房原本執行中的「一般常規性的護理衛教」。測量成效包括：口乾症狀問卷(Xerostomia Questionnaire)、美國國家癌症機構不良事件一般毒性標準第5版(NCI-CTCAE V5.0)之口腔黏膜炎分級、歐洲癌症治療及研究組織頭頸癌生活品質量表(EORTC QLQ H&N35)。由研究助理以Random Allocation Software Version1.1.0軟體進行區塊隨機分派至實驗組及控制組。實驗設計模式如圖二。

	組別	資料收集 T_0		資料收集 T_1		資料收集 T_2
	實驗組	O_1		O_2		O_3
	控制組	O_1	X	O_2	X	O_3

圖二、實驗設計模式以Random Allocation Software Version1.1.0軟體進行區塊隨機分派至實驗組及控制組。

一、控制組：本研究口腔癌患者，接受一般護理常規，沒有接受P-113噴劑者。

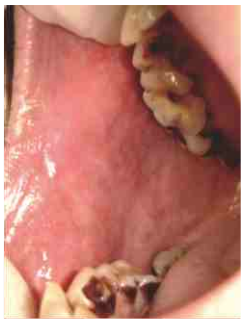
二、實驗組：本研究口腔癌患者，接受本次以P-113噴劑介入方案組別患者。

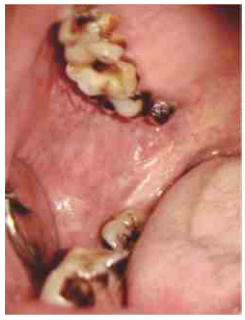
三、O_1：前測(口乾問卷、NCI-CTCAE V5.0 口腔黏膜炎分級表、EORTC QLQ-H&N35生活品質量表)

四、O_2：第1次後測 (介入第三週)

五、O_3：第2次後測 (介入第七週)

六、X： P-113噴劑介入方案 (本介入措施持續時間為七週，每日噴五次，分別為起床時、早餐後、午餐後、晚餐後、睡前，使用方式為噴嘴朝兩次口腔，每次按壓2～3下，口腔左右兩側各一次，噴灑完後，一小時內不能飲食喝水)





Results

本研究共招募94位受試者，其中符合篩選條件且願意參加試驗並完成同意書之填寫者共有80位，將研究對象分派至實驗組及控制組，實驗組及控制組各組人數皆為40位，並於P-113噴劑介入第三週及第七週進行後測。Table 4-1-1為實驗組及對照組之基本屬性分析，類別變項使用卡方值檢定，連續變項使用獨立樣本t檢定，其中對照組男性佔90%、女性佔10%，實驗組男性佔92.5%、女性佔7.5%，兩組性別分布無顯著差異(p = 1.0)；對照組未婚比例佔55%、已婚比例佔45%，實驗組未婚比例佔67.5%、已婚比例佔32.5%，兩組婚姻狀況無顯著差異(p = .251)；對照組無過去病史者佔2.5%、過去有一種慢性疾病者佔72.5%、有兩

種或兩種以上者佔25%，實驗組無過去病史者佔2.5%、過去有一種慢性疾病者佔75%、有兩種或兩種以上者佔22.5%，兩組過去病史無顯著差異(p = .966)；對照組沒有不健康的生活型態者佔37.5%、有不健康的生活型態者佔62.5%，實驗組沒有不健康的生活型態者佔55%、有不健康的生活型態者佔45%，兩組之生活型態分布無顯著差異(p = .116)；對照組無遠端轉移者佔95%、有遠端轉移者佔5%，實驗組無遠端轉移者佔97.5%、有遠端轉移者佔2.5%，分析兩組有無遠端轉移分布無顯著差異(p = .556)；對照組癌症分期為第一期者佔2.5%、第二期者佔35%、第三期者佔52.5%、第四期者佔10%；實驗組癌症分期為第二期者佔30%、第三期者佔62.5%、第四期者佔7.5%，兩組分析癌症分期分布無顯著差異(p = .649)；對照組癌症治療方式為放療者佔2.5%、化療合併手術者佔5%、放療合併化療及手術者佔92.5%，實驗組放療者佔2.5%、化療者佔2.5%、放療合併手術佔15%、化療合併手術者佔5%、放療合併化療及手術者佔75%，兩組治療方式分布無顯著差異(p = .102)；對照組平均年齡為50.05歲、實驗組平均年齡為51.43歲，兩組在年齡分布上無顯著差異(p = .461)；對照組平均教育年數約為6.6年、實驗組平均教育年數約為6.68年，兩組在教育年數分布上無顯著差異(p = .936)；對照組平均罹病時間為0.55年、實驗組平均罹病時間為1.10年，兩組在罹病時間分布上無顯著差異(p = .937)；口乾嚴重度對照組45.05、實驗組46.29，兩組在口乾嚴重度上無顯著差異(p = .539)；黏膜炎症狀嚴重度對照組1.65、實驗組1.875，兩組在黏膜炎症狀嚴重度分布無顯著差異(p = .106)；生活品質量表對照組72.51、實驗組69.16，兩組在生活品質分布上無顯著差異(p = .141)。

Table 4-1-1 Comparisons of the demographic data of the control group and experimental group at baseline (N = 80)

	CG (n = 40)		EG (n = 40)		χ^2	p
	n	%	n	%		
Gender					0.157	1.00
Male	36	90	37	92.5		
Female	4	10	3	7.5		
Marital status					1.317	.251
Single	22	55	27	67.5		
Married	18	45	13	32.5		
Past history					0.070	.966
No	1	2.5	1	2.5		
One chronic disease	29	72.5	30	75		
Two or more	10	25	9	22.5		
Unhealthy lifestyle					2.464	.116
No	15	37.5	22	55		
Yes	25	62.5	18	45		
Metastasis					0.346	.556
No	38	95	39	97.5		
Yes	2	5	1	2.5		
Cancer staging					1.645	.649
I	1	2.5	0	0		
II	14	35	12	30		
III	21	52.5	25	62.5		
IV	4	10	3	7.5		
Type of therapy					7.731	.102
Chemo	0	0	1	2.5		
RT	1	2.5	1	2.5		
RT and surgery	0	0	6	15		
Chemo and surgery	2	5	2	5		
CCRT and surgery	37	92.5	30	75		

	Mean	*SD*	*Mean*	*SD*	*t*	*p*
Age	50.05	8.73	51.43	7.83	.742	.461
Education (years)	6.60	4.26	6.68	4.05	.081	.936
Duration of illness	0.55	0.50	1.10	0.93	.080	.937
XQ	45.05	11.15	46.29	9.84	.146	.539
NCI-CTCAE V5.0	1.65	.622	1.875	.607	1.637	.106
QLQ H&N35	72.51	12.06	69.16	13.01	1.484	.141

Chemo, Chemotherapy; RT, radiation therapy; CCRT, Concurrent ChemoRadioTherapy; XQ, Xerostomia Qusetionnaire; NCI-CTCAE V5.0, National Cancer Institute - Common Terminology Criteria for Adverse Events Version 5.0; QLQ H&N35, Quality of Life Questionnaire Head and Neck Module 35.

Table 4-2-1 Effects of P-113 Peptide on the patients' Xerostomia Qusetionnaire

			95% Wald CI			
	B	*SE*	*Lower*	*Upper*	*Wald* χ^2	*p*
Intercept	42.94	1.90	39.21	46.66	509.72	< .00
Group	-0.66	1.44	-3.46	2.16	0.211	< .646
T_1	8.650	.8650	6.955	10.345	100.005	< .001
T_2	11.250	.5742	10.125	12.375	383.886	< .001
Group*T_1	6.325	1.1901	3.992	8.658	28.247	< .001
Group*T_2	-4.250	.8666	-5.948	-2.552	24.053	< .001

Covariates: gender, marital status, past history, unhealthy lifestyle, metastasis, cancer staging, type of therapy, age, years of education, duration of illness. P value: GEE(generalized estimating equations) to test the differences between the control group and the intervention group from baseline to the 3-week and 7-week follow up.

Table 4-3-1 Effects of P-113 Peptide on the patients' oral mucositis

			95% Wald CI			
	B	SE	Lower	Upper	Wald χ^2	*p*
Intercept	2.10	.45	1.21	2.98	21.55	< .001
Group	-.58	.15	-.88	-.28	14.40	< .001
T_1	-.37	.14	-.65	-.10	7.17	.007
T_2	.675	.1746	.333	1.017	14.946	< .001
Group*T_1	.775	.1887	.405	1.145	16.867	< .001
Group*T_2	.025	.2280	-.422	.472	.012	.913

Covariates: gender, marital status, past history, unhealthy lifestyle, metastasis, cancer staging, type of therapy, age, years of education, duration of illness. P value: GEE(generalized e stimating equations) to test the differences between the control group and the intervention group from baseline to the 3-week and 7-week follow up.

Discussion

本研究探討天然抗菌P-113胜肽噴劑介入對口腔癌患者的口乾症狀、口腔黏膜炎及生活品質改善成效。首先討論研究對象之基本屬性，接續討論P-113胜肽噴劑介入於口腔癌患者的口乾症狀、口腔黏膜炎及生活品質之成效。

口腔癌患者之基本屬性分布現況分析

本研究共有80位受試者，男性佔大多數為73位(佔91.3%)，女性為7位(佔8.7%)，為檢視對照組及實驗組的基本屬性在前測時是否存在差異，類別變項使用卡方值檢定，連續變項使用獨立樣本t檢定，基本屬性包含：性別、婚姻狀況、過去病史、生活型態、遠端轉移、癌症分期、治療方式等皆無顯著差異($p > .05$)，代表本研究人口基本屬性在基準值上為同質性。

P-113噴劑介入方案於口腔癌患者口乾症狀之成效分析

本研究結果顯示，P-113噴劑方案介入對口乾症狀改善達統計顯著差異，P-113噴劑介入於口腔癌患者之口乾程度使用口乾問卷(Xerostomia Qusetionnaire, XQ)，問卷內容包含：說話、咀嚼、吞嚥、睡眠、進食、未進食、喝水等8題進行評分，分數越高代表口乾症狀越嚴重(Eisbruch et al., 2001)。實驗組於介入三周後，較控制組多6.325分($B = 6.325, p < .001$)但是實驗組於介入7周後，較控制組多改善4.25分($B = -4.250, p < .001$)。控制組的口乾程度於第三周及第七周後皆比前測嚴重，整體而言，在接受P-113噴劑的患者之口乾症狀改善程度優於控制組。本研究結果與國外學者Gusman et al. (2001)的分析相近，因P-113胜肽結構特性易具有保濕功能，作用機制為能促進彈力纖維(elastic fibers)、膠原蛋白(collagen)和透明質酸(hyalouronic acid)增生，進而提高含水量，達到保濕功能，因此能針對口乾症狀進行改善，也與本研究結果相同。P-113噴劑介入方案於口腔癌患者生活品質之成效分析

控制基本屬性後，時間與組別的交互作用下，顯示頭頸癌生活品質疼痛次量表具有顯著差異，實驗組於介入七周後，較控制組改善11.67分($B = -11.67, p = .003$)，控制組於七周後，疼痛次量表的分數較前測多27.92分，由此可知隨著時間的變化下，P-113噴劑對於口腔癌患者之生活品質疼痛面向具有正面的影響。Rothstein 等人(2011)研究指出，P-113無法有效降低或舒緩疼痛感，與本研究結果不同，但在Bobek (2008)的研究中，研究結果顯示口乾症狀減緩有助於疼痛感的紓解，與本研究結果相符。

Conclusions

除了在疼痛次量表有顯著差異，在頭頸癌生活品質口乾次量表亦具有顯著差異，實驗組於介入七周後，較控制組改善17.5分($B = -17.5, p = .007$)，控制組於七周後，口乾次量表的分數較前測多34.17分，由此可知隨著時間的變化下，P-113噴劑對於口腔癌患者之生活品質口乾面向具有正面的影響。

參考文獻

1. 周繡玲. 臨床照護指引的發展方法. 腫瘤護理雜誌. 2011;11(增刊):5-14.

2.Figliolia SL, Oliveira DT, Pereira MC, Lauris JR, Mauricio AR, Oliveira DT, et al. Oral mucositis in acute lymphoblastic leukaemia: analysis of 169 paediatric patients. Oral Dis. 2008;14(8):761-6. Epub 2008/09/03. doi: 10.1111/j.1601-0825.2008.01468.x. PubMed PMID: 18761642.

3.陳嬿如、葉芳君、莊紫雲、林小玲. 化學治療癌症病人口腔黏膜炎發生率調查方案. 榮總護理. 2003;20(1):65-74.

4.Vagliano L, Feraut C, Gobetto G, Trunfio A, Errico A, Campani V, et al. Incidence and severity of oral mucositis in patients undergoing haematopoietic SCT--results of a multicentre study. Bone Marrow Transplant. 2011;46(5):727-32. Epub 2010/09/08. doi: 10.1038/bmt.2010.184. PubMed PMID: 20818449.

5.Potting CM, Mank A, Blijlevens NM, Donnelly JP, van Achterberg T. Providing oral care in haematological oncology patients: nurses' knowledge and skills. Eur J Oncol Nurs. 2008;12(4):291-8. Epub 2008/05/06. doi: 10.1016/j.ejon.2008.03.002. PubMed PMID: 18455960.

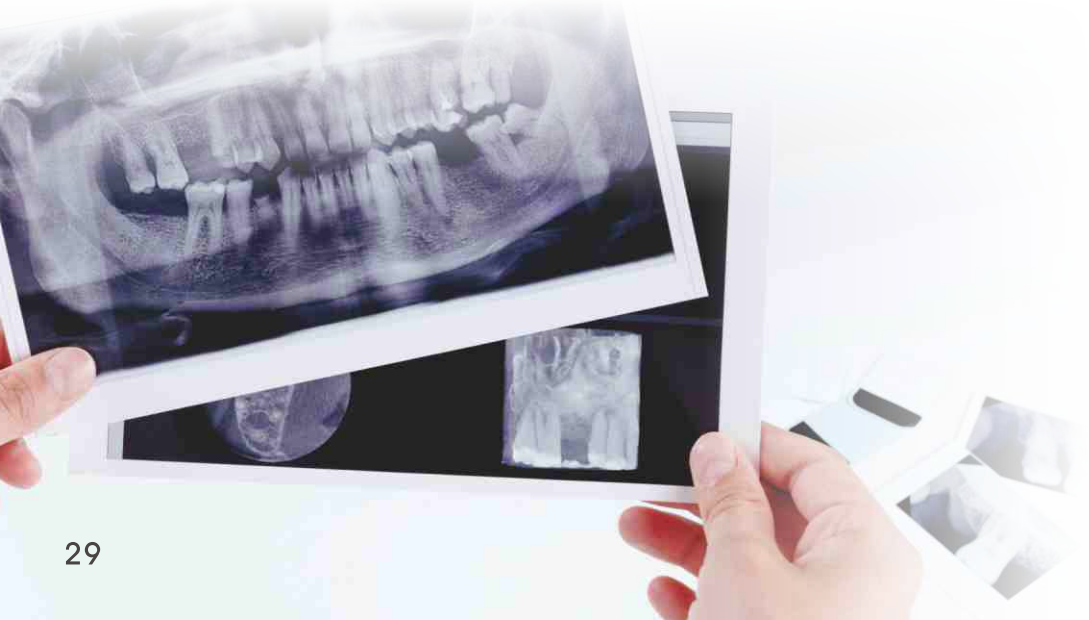
6.Quinn B, Potting CM, Stone R, Blijlevens NM, Fliedner M, Margulies A, et al. Guidelines for the assessment of oral mucositis in adult chemotherapy, radiotherapy and haematopoietic stem cell transplant patients. Eur J Cancer. 2008;44(1):61-72. Epub 2007/11/09. doi: 10.1016/j.ejca.2007.09.014. PubMed PMID: 17988858.

7.Brown CG, Wingard J. Clinical consequences of oral mucositis. Semin Oncol Nurs. 2004;20(1):16-21. Epub 2004/03/25. PubMed PMID: 15038513.

8.Glenny AM, Gibson F, Auld E, Coulson S, Clarkson JE, Craig JV, et al. The development of evidence-based guidelines on mouth care for children, teenagers and young adults treated for cancer. Eur J Cancer. 2010;46(8):1399-412. Epub 2010/03/17. doi: 10.1016/j.ejca.2010.01.023. PubMed PMID: 20227272.

9.Shih A, Miaskowski C, Dodd MJ, Stotts NA, MacPhail L. Mechanisms for radiation-induced oral mucositis and the consequences. Cancer Nurs. 2003;26(3):222-9. Epub 2003/07/02. PubMed PMID: 12832955.

10.Sonis ST. A biological approach to mucositis. J Support Oncol. 2004;2(1):21-32; discussion 5-6. Epub 2004/08/28. PubMed PMID: 15330370.



論文原稿

探討天然抗菌P-113胜肽噴劑介入改善口腔癌病人接受化放療前後的口乾症狀及口腔黏膜炎與生活品質的影響

The effects of P-113 peptide on improvement of xerostomia and oral mucositis to quality of life in oral cancer patients.

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Abstract

Background: Radiotherapy always cause some side effects, for example, xerostomia, mucositis, loss of taste, decayed tooth, hard to swallow. Radiation-induced toxicity can cause weakness, fatigue, decreased quality of life, an inability to tolerate treatment, and increased mortality.
Purposes: This study was to explore the effects of P-113 peptide on improvement of xerostomia and oral mucositis to quality of life in oral cancer patients.
Methods: A randomized controlled trial. Eighty participants were recruited and use the blocked randomization to assign them into the control group and the experimental group. The control group received routine care and the experimental gruop use the P-113.Data were collected at baseline, 3 weeks and 7 weeks after the intervention. The IBM SPSS 20.0 was to use to examine the effects with Generalized estimating equations.
Results: The results showed that the experimental group with Xerostomia significantly improved in the 7 weeks. ($p < .001$) However, no significant differences in improvement of oral mucositis between the control group and experimental group. The pain score of the experimental group after seven weeks was improved 11.67 points higher than the control group ($p = .003$)
Conclusion: P-113 can improve xerostomia and pain in oral cancer patients.

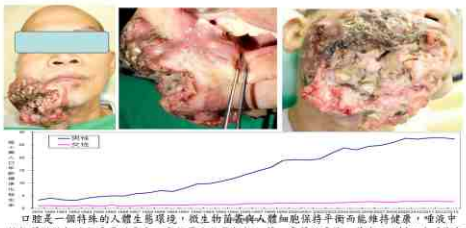
Keywords: head and neck cancer, radiochemotherapy, P-113 peptide, oral mucosa, quality of life

Introduction

口腔癌目前治療方式是以手術為主，在術後依照病理分期及相關危險因子來決定後續的放射線治療及化學治療，通常會進行大範圍的切除手術，一旦腫瘤及周遭組織被切除時，傷口重建決策也會隨之影響病人之吞咽功能，而癌症分期越高，對吞咽功能的影響也越大(相、胡，2017)。吞咽功能下降導致的吞咽困難除了會造成脫水、營養不均衡或吸入性肺炎等生理問題(蔡、陳，2013)，營養是健康的基礎，一旦病人的營養狀況改變，身體無法吸收充分的營養時，則會降低抵抗力，進一步導致其他併發症及死亡的發生率提升(涂，2008)，而嚴重的吞咽困難之病人則需要以鼻胃管灌食，但仍然有胃食道逆流及肺炎的危險，且病人無法與家人朋友一同進食，不但少了許多社交活動，也會對生活品質造成影響(賴、王、陳，2011)，口腔癌患者在接受不同的手術後，產生的副作用也不盡相同，而大部分的手術除了會改變患者的外表，同時也會影響其口腔的咀嚼功能，一旦咀嚼功能改變時，患者會變得十分困難甚至無法自行進食，可能導致其營養狀況也跟著改變，雖然在接受治療後，患者的壽命可以延長，但同時也可能造成其生理、心理、社會等層面的影響，除了疾病帶來的身體之不適，治療的過程同時也會造成患者的各層面之困擾，生活品質也隨之受到改變，因此不論是口腔癌或是手術及治療過程對患者來說，不但造成了身體之不適，更時時刻刻困擾著他們，其中常見的不適症狀有：味覺改變、口腔乾燥、患處疼痛、嘴巴潰瘍、噴嚏痛等，而這些症狀更嚴重降低患者進食的意願(Tomko et al., 2013)。從以上可以得知，口腔癌患者在術後除了需要面對自己的身體心像改變，也需要瞭解如何舒緩疾病及治療過程所帶來之不適，更需要家庭的支持及陪伴。

早期對於癌症病患的醫療較著重於患者壽命的延長，而現今則以提升患者的生活品質為目標，因此除了確認患者被哪些症狀所困擾著，也要緩解其症狀，同時瞭解患者的營養狀況，透過相關因素之探討，降低患者的症狀困擾，以提升患者進食之意願，進而改善其營養狀況，達到改善生活品質之目的，目前國內針對口腔癌患者的相關研究，較多提及症狀困擾與照護需求相關，較少探討患者經過放射線治療後的口乾症狀、口腔黏膜炎及其生活品質之影響，因此本研究欲透過早期介入，來改善口腔癌症因放射線或化學治療所引起的各種症狀，進而提升口腔癌病患的生活品質。

口腔癌為國人十大癌症排名中的第5名，更為男性排名中的第4名，台灣癌症登記中心統計分析國人口腔癌罹患率逐年上升，尤其在男性人口發生率由1979年3.28升高至2013年的27.41 **(圖一)**



口腔是一個特殊的人體生態環境，被生物菌叢與人體細胞保持平衡而能維持健康，唾液中的抗菌胜肽扮演很重要的角色，富組蛋白能夠抵抗細菌、真菌的感染，其中又以histatin 5具有最佳之抗菌作用，分析histatin 5中的不同組合片段，於全長24個胺基酸片段中又找出其中最短片段的12胺基酸，且具有最佳的抑菌作用之P-113 胜肽，其序列為AKRHHGYKRKFH-NH2 [13]，P-113 能阻礙白色念珠菌的單細胞(yeast)和菌絲體(mycelium)兩種型態的菌株生長；亦具有多種細菌之抑菌作用，抗真菌的機制為與菌體接受器結合進入菌內，在粗線體呼吸氧化過程中，將所產生的能量以電化學位能儲存於粗線體內膜，此過程稱之為 mitochondrial membrane potential (DYm)，以此進行電子傳遞鏈產生ATP以供細胞使用，致使菌體粗線體腫脹、克氏循環(Krebs cycle)因malate dehydrogenase的負調控(down regulation)而被抑制，F1F0-ATPase complex表現下降而使得ATP產量降低，另外，elongation factor alpha 的表現上升而使得代謝不協調而最終電子傳遞鏈失去效用而使菌體死亡。

P-113 抗菌胜肽來源為口腔中羊下腺和頜下腺共同分泌之histatin 5(富組蛋白)，於唾液中具有抑菌效果，能夠抑制白色念珠菌、新型隱球菌(Cryptococcus neoformans)和煙麴黴(Aspergillus fumigatus)等真菌感染，維護口腔健康。P-113即為histatin 5中的12個胺基酸片段，是由多個組氨酸等陽離子所組成之抗菌胜肽，能抑制白色念珠菌的單細胞(yeast)和菌絲體(mycelium)兩種型態的生長；亦具有多種細菌之抑菌作用。

Materials & Methods

本研究主要針對口腔癌患者提供P-113胜肽噴劑介入方案，期望可以達到下列目的：
一探討P-113胜肽噴劑介入方案於口腔癌患者的口乾症狀之成效。
二探討P-113胜肽噴劑介入方案於口腔癌患者的口腔黏膜炎與生活品質之成效。
三本研究為實驗性研究設計(Quasi-experimental design)，採立意取樣，以隨機分派至實驗組及控制組，採雙組前、後重複測量，採非干行式收集兩組資料，先進行實驗組收案並接受P-113噴劑方案，待實驗組所有資料收集完成後，再進行控制組收案，並接受兩原座本執行中的「一般常規性的護理衛教」。測量成效包括：口乾症狀問卷(Xerostomia Questionnaire)、美國國家癌症機構不良事件一般毒性標準第5版(NCI-CTCAE V5.0)之口腔黏膜炎分級、歐洲癌症治療及研究組織頭頸癌生活品質量表(EORTC QLQ H&N35)，由研究助理以Random Allocation Software Version1.1.0軟體進行區塊隨機分派至實驗組及控制組。實驗設計模式如圖二。

	組別	資料收集	介入	資料收集	介入	資料收集
	控制組	O_1		O_2		O_3
	實驗組	O_1	X	O_2	X	O_3

一控制組：本研究口腔癌患者，接受一般護理常規，沒有接受P-113噴劑者。
二實驗組：本研究口腔癌患者，接受本次以P-113噴劑介入方案組別患者。
三O_1：前測(口乾問卷、NCI-CTCAE V5.0口腔黏膜炎分級表、EORTC QLQ-H&N35生活品質量表)
四O_2：第1次後測 (介入第三週)
五O_3：第2次後測 (介入第七週)
六X：P-113噴劑介入方案 (本介入措施持續時間為七週，每日噴五次，分別為起床時、早餐後、午餐後、晚餐後、睡前，使用方式為噴霧朝兩次口腔，每次按壓2~3下，口腔左右兩側各一次，噴灑完後，一小時內不能飲食喝水)

Results

本研究共招募94位受試者，其中符合篩選條件且願意參加試驗並完成同意書之填寫者共有80位，將研究對象分派至實驗組及控制組，實驗組及控制組各組人數皆為40位，並於P-113噴劑介入第三週及第七週進行後測，*Table 4-1-1*為實驗組及對照組之基本屬性分析，類別變項使用卡方值檢定，連續變項使用獨立樣本t檢定，其中對照組男性佔90%、女性佔10%，實驗組男性佔92.5%、女性佔7.5%，兩組性別分布無顯著差異($p = 1.0$)；對照組未婚比例佔55%、已婚比例佔45%，實驗組未婚比例佔67.5%、已婚比例佔32.5%，兩組婚姻狀況無顯著差異($p = .251$)；對照組無過去病史者佔2.5%、過去有一種慢性疾病者佔72.5%、有兩種或兩種以上者佔25%，實驗組無過去病史者佔2.5%、過去有一種慢性疾病者佔75%、有兩種或兩種以上者佔22.5%，兩組過去病史無顯著差異($p = .966$)；對照組沒有不健康的生活型態者佔37.5%、有不健康的生活型態者佔62.5%，實驗組沒有不健康的生活型態者佔55%、有不健康的生活型態者佔45%，兩組之生活型態分布無顯著差異($p = .116$)；對照組無遠端轉移者佔95%、有遠端轉移者佔5%，實驗組無遠端轉移者佔97.5%、有遠端轉移者佔2.5%，分析兩組有無遠端轉移分布無顯著差異($p = .556$)；對照組癌症分期為第一期者佔2.5%、第二期者佔35%、第三期者佔52.5%、第四期者佔10%；實驗組癌症分期為第二期者佔30%、第三期者佔62.5%、第四期者佔7.5%，兩組分析癌症分期分布無顯著差異($p = .649$)；對照組癌症治療方式為放療者佔2.5%、化療合併手術者佔5%、放療合併化療及手術者佔92.5%，實驗組放療者佔2.5%、化療者佔2.5%、放療合併手術佔15%、化療合併手術者佔5%、放療合併化療及手術者佔75%，兩組治療方式分布無顯著差異($p = .102$)；對照組平均年齡為50.05歲、實驗組平均年齡為51.43歲，兩組在年齡分布上無顯著差異($p = .461$)；對照組平均教育年數約為6.6年、實驗組平均教育年數約為6.68年，兩組在教育年數分布上無顯著差異($p = .936$)；對照組平均罹病時間為0.55年、實驗組平均罹病時間為1.10年，兩組在罹病時間分布上無顯著差異($p = .937$)；口乾嚴重度對照組45.05、實驗組46.29，兩組在口乾嚴重度上無顯著差異($p = .539$)；黏膜炎症狀嚴重度對照組1.65、實驗組1.875，兩組在黏膜炎症狀嚴重度分布無顯著差異($p = .106$)；生活品質量表對照組72.51、實驗組69.16，兩組在生活品質分布上無顯著差異($p = .141$)。

Purpose

本研究探討天然抗菌P-113胜肽噴劑介入對口腔癌患者的口乾症狀、口腔黏膜炎及生活品質改善成效。首先討論研究對象之基本屬性，接續討論P-113胜肽噴劑介入於口腔癌患者的口乾症狀、口腔黏膜炎及生活品質之成效。

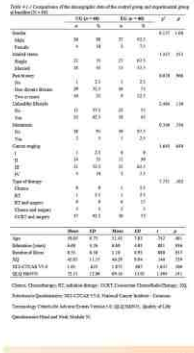
口腔癌患者之基本屬性分布現況分析

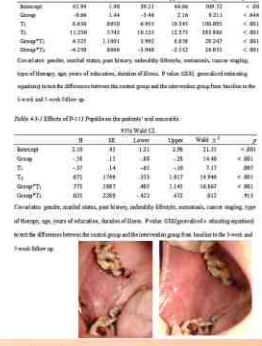
本研究共有80位受試者，男性佔大多數為73位(佔91.3%)，女性為7位(佔8.7%)，為檢視對照組及實驗組的基本屬性在前測時是否存在差異，類別變項使用卡方值檢定，連續變項使用獨立樣本t檢定，基本屬性包含：性別、婚姻狀況、過去病史、生活型態、追蹤轉移、癌症分期、治療方式等皆無顯著差異($p > .05$)，代表本研究入口基本屬性在基準值上為同質性。

P-113噴劑介入方案於口腔癌患者口乾症狀之成效分析

本研究結果顯示，P-113噴劑方案介入對口乾症狀改善達統計顯著差異，P-113噴劑介入於口腔癌患者之口乾程度使用口乾問卷(Xerostomia Qusetionnaire, XQ)，問卷內容包含：說話、咀嚼、吞嚥、睡眠、進食、未進食、喝水等8題進行評分，分數越高代表口乾症狀越嚴重(Eisbruch et al., 2001)。實驗組於介入三周後，較控制組多6.325分(B = 6.325, $p < .001$)但是實驗組於介入7周後，較控制組多改善4.25分(B = -4.250, $p < .001$)，控制組的口乾程度於第三周及第七周後皆比前測嚴重，整體而言，在接受P-113噴劑的患者之口乾症狀改善程度優於控制組。本研究結果與國外學者Gusman et al. (2001)的分析相近，因P-113胜肽結構特性易具有保濕功能，作用機制為能促進彈力纖維(elastic fibers)、膠原蛋白(collagen)和透明質酸(hyaluronic acid)增生，進而提高含水量，達到保濕功能，因此能針對口乾症狀進行改善，也與本研究結果相同，P-113噴劑介入方案於口腔癌患者生活品質之成效分析

控制基本屬性後，時間與組別的交互作用下，顯示頭頸癌生活品質疼痛次量表具有顯著差異，實驗組於介入七周後，較控制組改善11.67分(B = -11.67, p = .003)，控制組於七周後，疼痛次量表的分數較前測多27.92分，由此可知隨著時間的變化下，P-113噴劑對於口腔癌患者之生活品質疼痛面向具有正面的影響。Rothstein 等人(2011)研究指出，P-113無法有效降低或舒緩疼痛感，與本研究結果不同，但在Bobek (2008)的研究中，研究結果顯示口乾症狀減緩有助於疼痛感的紓解，與本研究結果相符。





Conclusions

除了在疼痛次量表有顯著差異，在頭頸癌生活品質口乾次量表亦具有顯著差異，實驗組於介入七周後，較控制組改善17.5分(B = -17.5, p = .007)，控制組於七周後，口乾次量表的分數較前測多34.17分，由此可知隨著時間的變化下，P-113噴劑對於口腔癌患者之生活品質口乾面向具有正面的影響。

學術專題

2020年度 大會壁報論文比賽作品欣賞 醫院組—第二名

分析小臼齒牙根以探討椎狀植體之收斂角度

The exploration of the convergent angles of tapered implants with analysis of bicuspid roots

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Introduction

Tapered implants are cylindrical implants, and whether the taper position is at the cervical, middle, or apical parts of the implant body, the diameter at the apical end is narrower than that at the crestal bone level. Consequently, tapered implants also include implants with a continuously or a non-continuously convergent body corono-apically.1 Clinically, tapered implants with assorted conical angles are available. Tapered implants were used in soft bone to increase the primary stability and in imperfect anatomical conditions, such as facial undercuts, converging roots tip, concave jaw structure or narrow atrophic ridges to avoid further surgical complexity.2-4 However, few studies have discussed the issues of implants with a continuously increasing taper slope (TS) and convergent angle (CA), or the theories and original sources of CA.

Generally, the taper angle was defined as a slope formed by the decreasing radiuses toward the apex of teeth and implants; the CA represented the narrowing diameters molded by two corresponding taper angles. The aims of this study were to measure the root surface areas (RSA), calculate the radius/diameters (R/D) of the premolar roots, and analyze the TS/CA of tooth roots.

Material and Methods

A total of 73 human single-rooted premolars (35 maxillary and 38 mandibular premolars obtained from patients aged from 18-65 of both genders who underwent orthodontic and/or periodontal treatment in the Dental Department) were scanned by a micro-computed tomography (micro-CT; SkyScan 1076, Bruker) and then analyzed and converted with DataViewer, CTVol and CTVox software (Bruker). Subsequently, Pro/ENGINEER software (PTC, Needham) was applied to do the further survey. (Fig. 1)

The root length (RL) was the joint of the root apex and the cementoenamel junction (CEJ), and the premolar CEJ was the midpoints of mesiodistal to the buccolingual CEJ lines. Root surface area (RSA), radius/diameter (R/D) and TS/CA at the planned 1st to 10th mm corono-apical levels were calculated and statistically analyzed using independent t-test, paired t-test and One-way ANOVA. The significance was set at the level of $p<0.05$.

Results

The horizontal cross-sectional images of each analyzed tooth were put together and converted into a 3D structure (Fig. 1).

The examined mandibular and maxillary premolars showed a wide range variation in RSA and RL measurements and comparisons (Table 1, $p < 0.05$). Additionally, the maxillary and mandibular premolars demonstrated significant differences in radius(R), diameter (D), and RSA measurements at the most corresponding PALs that assessed in millimeter corono-apically. For every 1.0 mm corono-apical measurement, the R/D of the maxillary premolar roots gradually decreased from 4.12/8.24 mm to 2.13/4.33 mm, and the R/D of the mandibular roots gradually decreased from 3.67/7.34 mm to 2.01/4.02 mm. (Table 1)

Generally, the TSs and CAs formed by 2 subsequent corono-apical R/Ds measured in every 1.0 mm presented a non-significant difference between the R/Ds of the maxillary and mandibular premolars except for the comparison of the 1st and 2nd coronal R/Ds in the mandibular group (Table 2).

However, the TS/CA comparisons based on 2 corono-apical R/Ds measurements in every 1.0 to 9.0 mm showed an insignificant variation for maxillary premolars and a significant difference for mandibular premolars (Table 3). Only two subsequent corono-apical R/Ds were compared in every 8.0 mm and 1 value for every 9.0 mm measurement was achieved. Therefore, these 3 values were managed together because they were in the same catalogue for both of the maxillary and mandibular premolar groups (Table 3).

Correspondingly, in every 1.0 mm to 8.0/9.0 mm measurement, the corono-apical TS/CA records of the maxillary premolar ranged from 17.5o/29.4o to 11.8o/22.5o, and that of the mandibular premolar varied from 15.3o/26.6o to 10.2o/19.6o. The TS/CA of the maxillary and mandibular premolars showed a significant variation in all measurements from 1.0 mm to 8.0/9.0 mm. The premolars of both arches showed an incomparable pattern of TS/CA evolvement and demonstrate dissimilar declining patterns (Table 3).

Accordingly, there were no significant differences between RSA of actual measurement and TS/CA cone-shaped calculation on both maxillary and mandibular premolars (Table 4). It revealed a proper transformation of the natural root form into a cone-shaped form.

Discussion

This study only surveyed 10 mm root structure apical to CEJ to avoid analyzing the morphologic variation at root apexes of bicuspids, which could cause extensive bias. The complex size and morphology of the premolar roots, convoluted CEJ anatomy and varied RL explained the wide range of SD distribution in every 1.0 mm and 2.0 mm corono-apical measurement, especially for the area 2.0 mm apical to CEJ. The modified R/Ds in this premolar survey were wider than the implant diameter routinely used in dental clinics; the ridge resorption after tooth extraction could describe the necessary diameter reduction for commercial implants insertion.

A comparable success rate was noted between parallel-walled and tapered implants;

however, the tapered implants gained an insignificant higher implant stability values than parallel-walled implants in a short-term survey.5 In addition, clinical study presented that parallel-walled implants lost significantly more marginal bone than tapered implants.6

The pattern of force distribution along the tapered implants with multiple TS/CAs could be significantly different from that with single TS/CA, and the responses of surrounding crestal bone to the loading forces could also be substantially diverse. Further studies are required to elucidate the mechanism of stress/strain distribution around various TS/CA implants.

Limitations of this study include: 1) a wide anatomical variation of the premolars, especially the tooth structure at CEJ, which may affect measurement and result in some deviation; 2) the sample size was small and might cause a statistical deviation; 3) the buccolingual and mesiodistal TS/CA measurements of the premolar roots were not included and could be significantly different from the calculated averages; 4) the mismatch of the actual irregular shape of natural premolar's perimeter and the representative circle could be a bias to the results; 5) the information of incisors, canines and molars should be considered as the anatomical forms of these teeth are so diverse that the examined results could be independent.

Conclusion

The gradual reduction of the tapered premolar roots is significant for the mandible and insignificant for the maxilla. This study concluded that a tapered implant with a regular form mimicking maxillary premolar roots could appear as a conical shape with constant TS. However, the implant simulating the mandibular premolar root could converge corono-apically with a variable TS rather than bearing a cylindrical or conical feature. Based on the obtained TS/CAs, the studies about the associated bone remodeling, and how the occlusal forces distribute onto the crestal bone or latero-apically to supporting alveolar bone according to these obtained TS/CAs are indicated to further elucidate the superiority of tapered implants mimicking natural roots.

References

1.Jokstad A, Ganeles J. Systematic review of clinical and patient-reported outcomes following oral rehabilitation on dental implants with a tapered compared to a non-tapered implant design. Clin Oral Implants Res 2018;29 Suppl 16:41-54.

2.Alves CC, Neves M. Tapered implants: from indications to advantages. Int J Periodontics Restorative Dent 2009;29:161-7.

3.O'Sullivan D, Sennerby L, Meredith N. Influence of implant taper on the primary and secondary stability of osseointegrated titanium implants. Clin Oral Implants Res 2004;15:474-80.

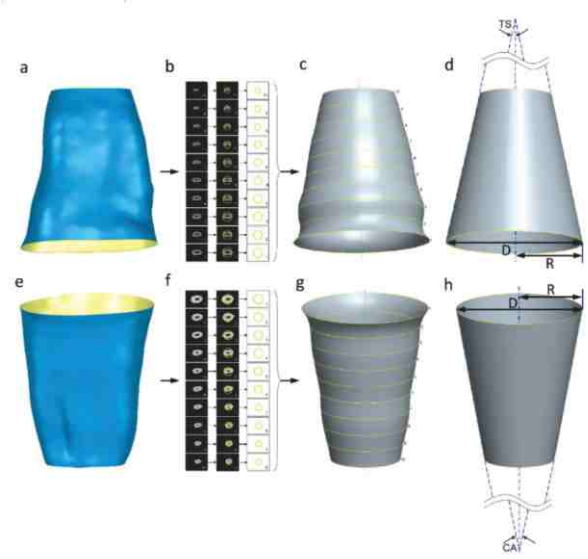
4.Martinez H, Davarpanah M, Missika P, Celletti R, Lazzara R. Optimal implant stabilization in low density bone. Clin Oral Implants Res 2001;12:423-32.

5.Norton MR. Marginal bone levels at single tooth implants with a conical fixture design. The influence of surface macro- and microstructure. Clin Oral Implants Res 1998;9:91-9.

6.Atieh MA, Alsabeeha N, Duncan WJ. Stability of tapered and parallel-walled dental implants: A systematic review and meta-analysis. Clin Implant Dent Relat Res 2018;20:634-45.

Figure and figure legends

Figure 1. 3D TS/CA models of maxillary premolars (a-d) and mandibular premolars (e-h).



(a and e): Converted STL images of selected premolar sections.
(b and f): Series cross section of premolars with irregular shape of perimeter from 1st mm to 10th mm below CEJ were modified into a corresponding circles outline.
(c and g): Root morphology based on reconstructing individual cross sections of B & F.
(d and h): Cone shape configuration according to the average TS/CA of maxillary and mandibular premolars.

D: Diameter; R: Radius; TS: Taper Slope (decided by the decreasing radiuses); CA: Convergent Angle (corresponding to the narrowing diameters)

Tables

Table 1. Amount of RSA, Radius and Diameter at evaluated PALs corono-apically.

	Maxillary premolars (n=35)		Mandibular premolars (n=38)		Max. vs. Mand.
	Mean ± SD	95% CI	Mean ± SD	95% CI	$p < 0.05$
100% RSA	222.97 ± 33.56 mm^2	211.44 ~ 234.49	202.26 ± 24.86 mm^2	194.09 ~ 210.43	0.004
Root length	12.45 ± 1.14 mm	12.06 ~ 12.84	13.28 ± 1.56 mm	12.77 ~ 13.80	0.011
RSA, R & D					
CEJ - 1st mm RSA	26.02 ± 4.74 mm^2	24.45 ~ 27.59	23.40 ± 2.19 mm^2	22.70 ~ 24.09	< 0.001
R at 0.5 mm PAL	4.12±0.43 mm	3.97~4.27	3.67±0.25 mm	3.58~3.75	< 0.001
D at 0.5 mm PAL	8.24±0.85 mm	7.93~8.54	7.34±0.50 mm	7.17~7.51	< 0.001
1st- 2nd mm RSA	23.21 ± 3.59 mm^2	22.02 ~ 24.40	20.26 ± 1.69 mm^2	19.73 ~ 20.80	< 0.001
R at 1.5 mm PAL	3.69±0.30 mm	3.58~3.80	3.20±0.21 mm	3.13~3.27	< 0.001
D at 1.5 mm PAL	7.45±0.67 mm	7.21~7.69	6.41±0.41 mm	6.27~6.55	< 0.001
2nd - 3rd mm RSA	23.86 ± 4.09 mm^2	22.51 ~ 25.22	19.44 ± 3.29 mm^2	18.40 ~ 20.49	< 0.001
R at 2.5 mm PAL	3.79±0.49 mm	3.61~3.97	3.10±0.26 mm	3.00~3.19	< 0.001
D at 2.5 mm PAL	7.40±0.82 mm	7.08~7.71	6.25±0.61 mm	6.04~6.46	< 0.001
3rd - 4th mm RSA	21.90 ± 2.57 mm^2	21.05 ~ 22.75	18.88 ± 1.90 mm^2	18.28 ~ 19.49	< 0.001
R at 3.5 mm PAL	3.52±0.37 mm	3.39~3.65	2.95±0.22 mm	2.87~3.03	< 0.001
D at 3.5 mm PAL	6.96±0.70 mm	6.71~7.21	5.91±0.45 mm	5.76~6.06	< 0.001
4th - 5th mm RSA	20.87 ± 3.90 mm^2	19.58 ~ 22.17	18.17 ± 3.77 mm^2	16.97 ~ 19.37	0.004
R at 4.5 mm PAL	3.31±0.43 mm	3.15~3.46	2.82±0.25 mm	2.74~2.91	< 0.001
D at 4.5 mm PAL	6.52±1.01 mm	6.17~6.87	5.70±0.57 mm	5.50~5.89	< 0.001

	Maxillary premolars (n=35)		Mandibular premolars (n=38)		Max. vs. Mand.
5th - 6th mm RSA	19.41 ± 4.32 mm²	17.08 ~ 20.85	16.75 ± 2.39 mm²	15.99~ 17.50	0.002
R at 5.5 mm PAL	3.11±0.48 mm	2.94~3.28	2.60±0.27 mm	2.51~2.69	< 0.001
D at 5.5 mm PAL	6.22±0.96 mm	5.87~6.56	5.21±0.54 mm	5.02~5.39	< 0.001
6th - 7th mm RSA	18.56 ± 4.23 mm²	17.16 ~ 19.96	16.67 ± 2.53 mm²	15.86 ~ 17.47	0.022
R at 6.5 mm PAL	2.95±0.42 mm	2.80~3.10	2.59±0.29 mm	2.49~2.69	< 0.001
D at 6.5 mm PAL	5.91±0.84 mm	5.61~6.21	5.18±0.58 mm	4.98~5.37	< 0.001
7th - 8th mm RSA	17.14 ± 4.48 mm²	15.66 ~ 18.63	16.12 ± 3.65 mm²	14.96 ~ 17.28	0.286
R at 7.5 mm PAL	2.70±0.55 mm	2.50~2.90	2.45±0.31 mm	2.35~2.56	0.031
D at 7.5 mm PAL	5.44±1.23 mm	4.99~5.88	4.86±0.55 mm	4.67~5.05	0.019
8th - 9th mm RSA	16.50 ± 4.34 mm²	15.07 ~ 17.94	14.28 ± 3.25 mm²	13.18 ~ 15.37	0.017
R at 8.5 mm PAL	2.52±0.53 mm	2.33~2.70	2.18±0.38 mm	2.05~2.30	0.003
D at 8.5 mm PAL	5.02±1.07 mm	4.63~5.41	4.41±0.68 mm	4.18~4.65	0.008
9th - 10th mm RSA	13.61 ± 3.99 mm²	12.29 ~ 14.93	13.38 ± 4.97 mm²	11.80 ~ 14.95	0.833
R at 9.5 mm PAL	2.13±0.60 mm	1.92~2.34	2.01±0.37 mm	1.88~2.14	0.335
D at 9.5 mm PAL	4.33±1.27 mm	3.90~4.77	4.02±0.73 mm	3.76~4.28	0.217

D: diameter, Mand.: mandibular, Max.: maxillary, R: radius,
PAL: Periodontal attachment level measured in millimeter (mm) from CEJ to 10th mm.
RSA: Root surface area determined by a 3–D image and measured in mm corono-apically.
Repeated measures analysis of variance (RMAV) revealed if the amount of RSA at surveyed PALs were in 95% confidence intervals (CI).
Independent t test was applied for maxillary R/D and mandibular R/D comparison at corresponding levels: *: $p < 0.05$, **: $p < 0.01$, ***: $p < 0.001$

Table 2. TS and CA formed by 2 subsequent R/Ds in every 1.0 mm measurement corono-apically.

TS & CA formed by various R/Ds		Maxillary: Mean ± SD & Sig. b/w 2 levels (*P< 0.05*)		Mandible: Mean ± SD & Sig. b/w 2 levels (*P< 0.05*)		Max. vs. Mand. *P< 0.05 (%)*
1st – 2nd R/D	**TS**	21.79 ± 9.48	0.250	24.92 ± 9.32	< 0.001	*P= 0.214*
	CA	35.25 ± 11.34	0.249	40.79 ± 12.36	< 0.001	P= 0.098
2nd – 3rd R/D	**TS**	16.95 ± 6.04	0.400	14.54 ± 8.40	0.510	*P= 0.405*
	CA	31.02 ± 8.88	0.776	25.26 ± 13.32	0.853	P= 0.234
3rd – 4th R/D	**TS**	20.03 ± 12.90	0.228	15.02 ± 8.23	0.202	*P= 0.132*
	CA	27.23 ± 13.22	0.723	27.10 ± 12.37	0.182	P= 0.974
4th – 5th R/D	**TS**	14.71 ± 8.76	0.671	11.12 ± 6.04	0.634	*P= 0.125*
	CA	27.65 ± 13.51	0.656	20.88 ± 9.93	0.610	P= 0.072
5th – 6th R/D	**TS**	13.78 ± 7.88	0.086	12.92 ± 6.39	0.011	*P= 0.674*
	CA	26.00 ± 11.79	0.107	23.96 ± 10.39	0.010	*P= 0.528*
6th – 7th R/D	**TS**	16.24 ±7.25	0.669	10.83 ± 2.87	0.236	*P= 0.003*
	CA	29.34 ± 11.61	0.657	20.82 ± 5.14	0.220	P=0.004

TS & CA formed by various R/Ds		Maxillary: Mean ± SD & Sig. b/w 2 levels (*P< 0.05*)		Mandible: Mean ± SD & Sig. b/w 2 levels (*P< 0.05*)		Max. vs. Mand. *P< 0.05 (%)*
7^{th} – 8^{th} R/D	TS	17.10 ± 8.33	0.719	13.82 ± 7.81	0.599	*P= 0.175*
	CA	30.46 ± 13.14	0.743	24.44 ± 9.94	0.868	*P= 0.092*
8^{th} – 9^{th} R/D	TS	16.67 ± 7.07	0.313	13.83 ±7.36	0.791	*P= 0.191*
	CA	29.44 ± 11.83	0.670	23.22 ± 7.61	0.355	*P=0.065*
9^{th} – 10^{th} R/D	TS	18.86 ± 12.17	-	14.38 ± 6.73	-	*P= 0.129*
	CA	28.04 ± 15.54	-	26.39 ±10.79	-	*P= 0.688*

R/D: radius/diameter, Sig. b/w 2 levels: significance between this and the following TS/CA.
TS: taper slope formed according to 2 subsequent radiuses.
CA: convergent angle molded by 2 subsequent diameters.
Independent t test was applied for maxillary TS/CA and mandibular TS/CA comparison at corresponding levels: *: $p < 0.05$, **: $p < 0.01$, ***: $p < 0.001$
Paired t test was used to examine the TS/CA significances of 2 sequentially corono-apical levels: *: $p < 0.05$, **: $p < 0.01$, ***: $p < 0.001$

Table 3. TS and CA measured in every 1.0 mm to 9.0 mm measurement according to various R/Ds

TS & CA at various measurements in		Maxillary: Mean ± SD & Sig. b/w levels (*p< 0.05*)		Mandible: Mean ± SD & Sig. b/w levels (*p< 0.05*)		Max. vs. Mand. *p< 0.05 (%)*
every 1.0 mm	TS	17.47 ± 9.38	0.233	15.26 ± 8.51	< 0.001	0.014
	CA	29.36 ± 12.63	0.438	26.63 ± 12.16	< 0.001	0.032
every 2.0 mm	TS	14.36 ± 7.82	0.769	11.79 ± 6.11	< 0.001	< 0.001
	CA	25.34 ± 10.74	0.468	22.17 ± 9.87	< 0.001	0.003
every 3.0 mm	TS	13.70 ± 6.92	0.373	10.61 ± 4.25	< 0.001	< 0.001
	CA	25.10 ± 10.92	0.376	20.30 ± 6.99	< 0.001	< 0.001
every 4.0 mm	TS	12.68 ± 5.86	0.368	10.07 ± 3.53	< 0.001	< 0.001
	CA	24.13 ± 9.54	0.265	19.40 ± 5.94	< 0.001	< 0.001
every 5.0 mm	TS	12.85 ± 5.15	0.066	9.89 ± 3.28	< 0.001	< 0.001
	CA	23.67 ± 8.51	0.051	19.05 ± 5.66	< 0.001	< 0.001
every 6.0 mm	TS	12.51 ± 4.33	0.074	9.46 ± 2.68	< 0.001	< 0.001
	CA	23.28 ± 7.18	0.580	18.34 ± 4.59	< 0.001	< 0.001
every 7.0 mm	TS	12.20 ± 4.24	0.109	9.69 ± 2.44	0.031	< 0.001
	CA	22.88 ± 6.91	0.558	18.74 ± 4.39	0.009	< 0.001
every 8mm to 9mm	TS	11.80 ± 3.74	0.901	10.21 ± 2.41	0.004	0.001
	CA	22.52 ± 6.50	0.981	19.59 ± 4.23	0.005	< 0.001

TS & CA at various measurements in		Maxillary: Mean ± SD & Sig. b/w levels ($p< 0.05$)		Mandible: Mean ± SD & Sig. b/w levels ($p< 0.05$)		Max. vs. Mand. $p< 0.05$ (%)
Average	TS	13.44 ± 6.31 (13.27 ± 6.11)	< 0.001$^{\Phi}$	11.25 ± 5.48 (10.87 ± 4.81)	< 0.001$^{\Phi}$	< 0.001
	CA	24.53 ± 9.44 (24.31 ± 9.27)	< 0.001$^{\Phi}$	21.06 ± 8.39 (20.55 ± 7.61)	< 0.001$^{\Phi}$	< 0.001

R/D: radius/diameter
CA: convergent angle,
TS: taper slope. (CA TS2)
Independent t test was applied for maxillary TS/CA and mandibular TS/CA comparison at corresponding levels: *: $p < 0.05$, **: $p < 0.01$, ***: $p < 0.001$
One-way ANOVA was used to examine the TS/CA significances at various measurements corono-apically: *: $p < 0.05$, **: $p < 0.01$, ***: $p < 0.001$
$^{\Phi}$: Significances between the measured angles and 0° (cone vs. cylinder shape).
*: $p < 0.05$, **: $p < 0.01$, ***: $p < 0.001$

Table 4. RSA from CEJ to 10th mm by actual measurement or by TS/CA cone shape calculation.

	Maxillary premolars (n=35)		Mandibular premolars (n=38)		Max. vs. Mand.
	Mean ± SD	Sig. b/w 2 methods ($P< 0.05$)	Mean ± SD	Sig. b/w 2 methods ($P< 0.05$)	$P < 0.05$
CEJ - 10th mm RSA actual measurement	201.09 ± 23.71 mm^2		177.34 ± 19.98 mm^2		< 0.001
		0.777		0.105	
CEJ - 10th mm RSA TS/CA cone-shape calculation	203.21 ± 37.39 mm^2		187.20 ± 31.16 mm^2		< 0.001

Independent t test was applied for maxillary RSA and mandibular RSA comparison at corresponding levels: *: $p < 0.05$, **: $p < 0.01$, ***: $p < 0.001$
Paired t test was used to examine the RSA by actual and cone-shape measurement: *: $p < 0.05$, **: $p < 0.01$, ***: $p < 0.001$

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MRONJ in Prostate Cancer Patient: A Case Report

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Division of Oral and Maxillofacial Surgery, Department of Dentistry,
Taoyuan General hospital , Taoyuan, Taiwan.

Introduction

Medication-related osteonecrosis of the jaw (MRONJ) is defined by AAOMS in 2008 known as a side-effect of antiresorptive and angiogenic inhibitor therapy. Patients with malignant diseases such as breast cancer, prostate cancer, and multiple myeloma may use antiresorptive or angiogenic inhibitor for treatment of bone metastasis. In 2018, Multinational Association of Supportive Care in Cancer /International Society of Oral Oncology(MASCC/ISOO) has released a practice guideline for prevention and management of MRONJ in patients with cancer. In this case report, we present an MRONJ case with prostate cancer and how we utilized this guideline on this patient.

Case Presentation

Present illness: A 74-year-old male came to Taoyuan General Hospital for pain and swelling over right mandible for 3 weeks.

Review of system: Prostate cancer.

Past medical history: Xgyva injection for 1.5 years. No radiotherapy history.

Physical examination: Exposed necrotic bone over right mandible with granulation tissue.(Fig.1)

Incisional biopsy: Necrotic bone.

Diagnosis: MRONJ over right mandible.

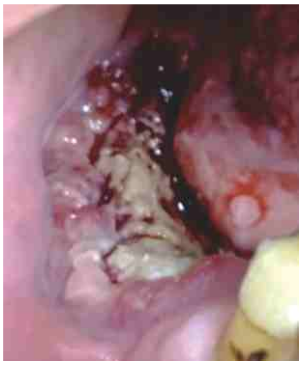
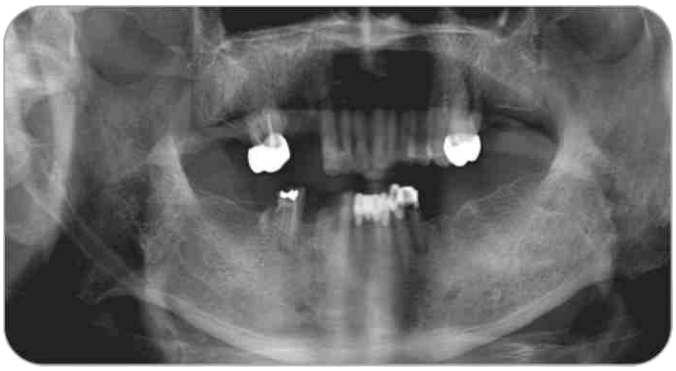


Fig.1

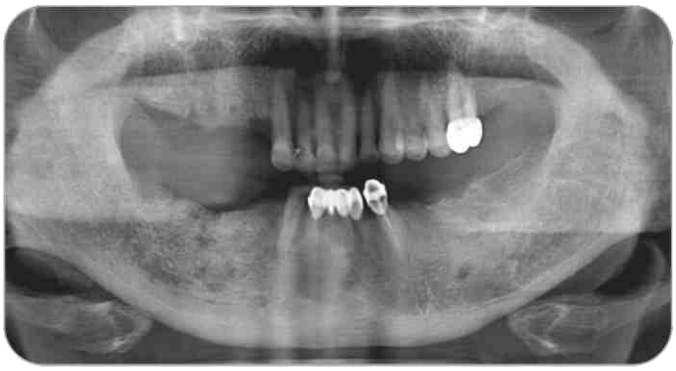
Treatment points:

1. According to MASCC guideline, anti-resorptive medication (Xgyva) was paused.
2. Conservative treatment was arranged. Daily irrigation for infection control with Chlorohexidine and debridement of necrotic bone with minimally aggressive method.
3. Oral hygiene care. Keep oral hygiene of other teeth for infection control.
4. Pain control. Analgesics prescribed.
5. Family support. The pain and discomfort unhealed wound cause physical and mental problem to patient.

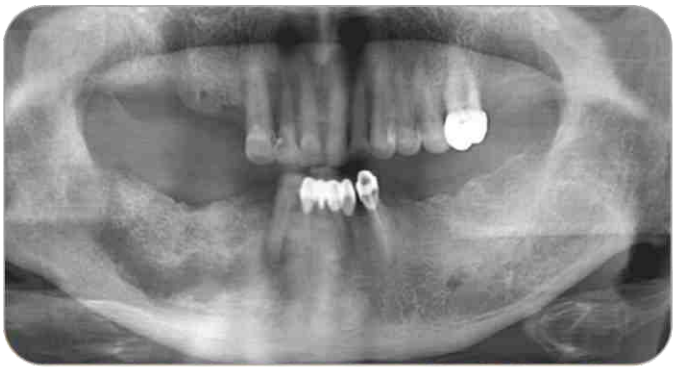
Radiographic finding: The panoramic radiography showed the progression of MRONJ in this case.



1 year before the MRONJ onset, Xgyva injection for 6 months



8 weeks after bone exposure. The image showed an irregular bony lesion without clear margin over right mandible.



◀ 16 weeks after bone exposure. An irregular bony segment with clear margin separated from right mandible.

Surgery procedure:

Under general anesthesia, we performed sequestrectomy over right mandible(Fig.2). The remaining mandible was covered by new-generated granulation tissue(Fig.3). Specimen sized 5x2x2.5cm(Fig.4).

Post-operation:

(1)The pathologic report showed sequestrum without metastasis.

(2)Post-operative 1 week panoramic film showed no necrotic bone of remaining mandible(Fig.5).

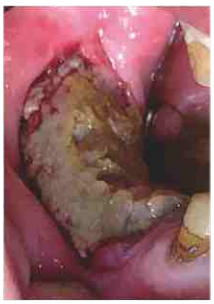


Fig.2

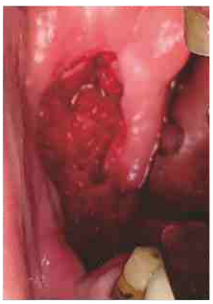


Fig.3

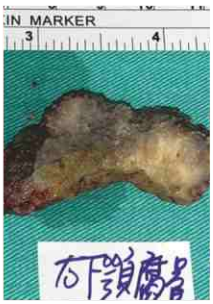
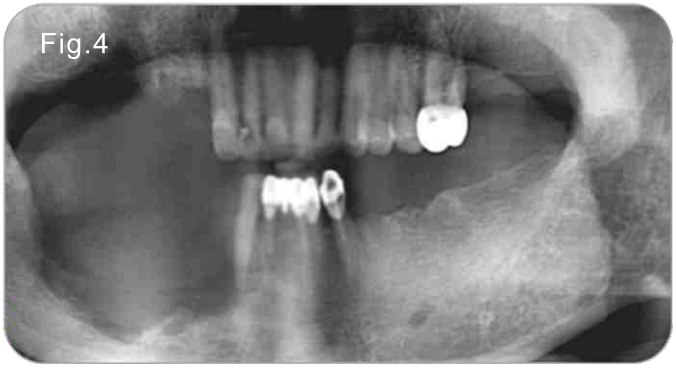


Fig.4



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Treatment of MRONJ is a demanding challenge for clinicians. There are different strategy and an effective and appropriate MRONJ therapy is still to be decided. From the guideline, it is suggested that a multidisciplinary team approach including a dentist, an

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Reference

1. Oral and Maxillofacial Pathology, third edition
2. Ruggiero SL, Dodson TB, Fantasia J, et al: American Association of Oral and Maxillofacial Surgeons position paper on medication-related osteonecrosis of the jaw—2014 update. J Oral Maxillofac Surg 72:1938-1956, 2014 [Erratum: J Oral Maxillofac Surg 73:1879, 2015; J Oral Maxillofac Surg 73:1440, 2015
3. Noam Yarom, DMD, Medication-Related Osteonecrosis of the Jaw: MASCC/ISOO/ASCO Clinical Practice Guideline. J Clin Oncol. 2019 Sep 1;37(25):2270-2290.

論文原稿

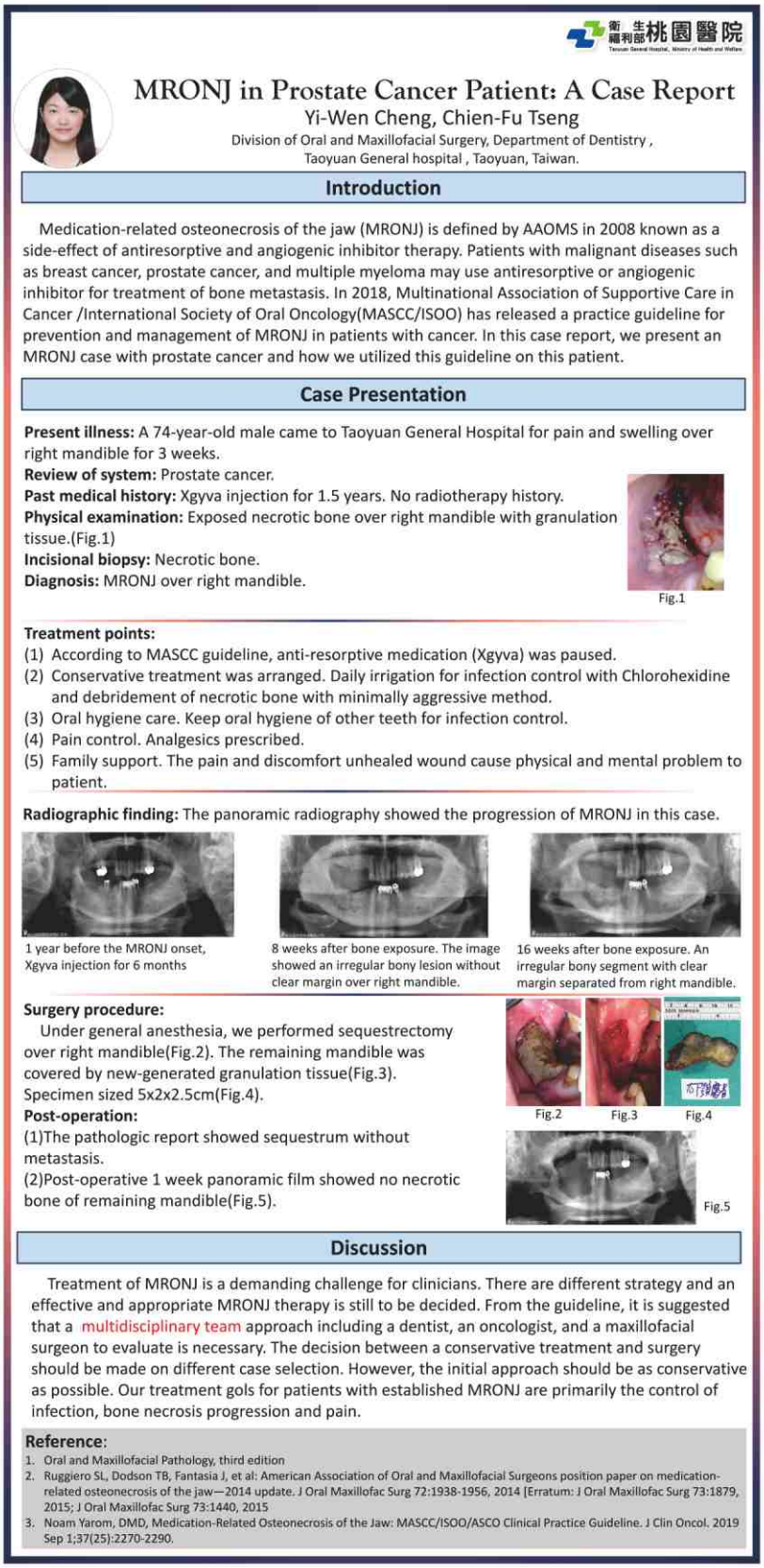

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Fig.2 Fig.3 Fig.4

Fig.5

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