

## 第25屆大會壁報論文比賽 **醫院組** 第一名

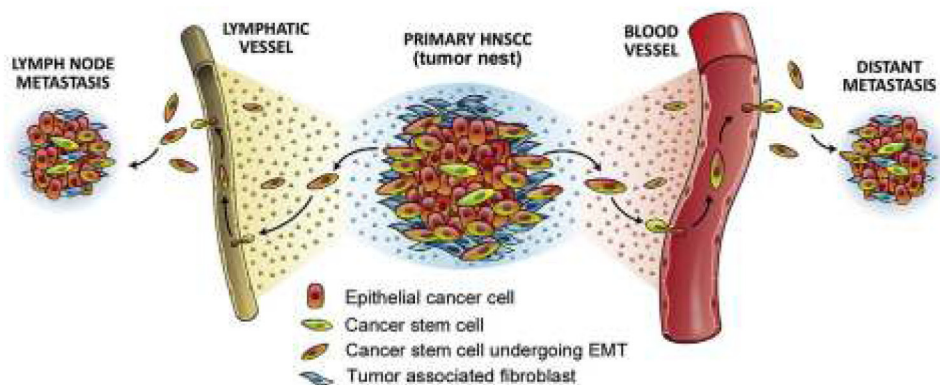
### ***A model of rapid sphere formation with Cancer stem cell properties in head and neck cancer***

Chien-Fu Tseng<sup>1,2,3</sup> Hsin-Ming Chen<sup>2,3</sup> Sang-Heng Kok<sup>2,3</sup> **曾建福 醫師**

1. Department of Oral and Maxillofacial Surgery, Tao-Yuan General Hospital
2. Department of Oral and Maxillofacial Surgery, National Taiwan University Hospital and
3. School of Dentistry, National Taiwan University, Taipei, Taiwan, R.O.C.

#### Introduction

Oral submucous fibrosis is an oral potentially malignant disorders (PMD) disease. Based case control study and other epidemiological studies, OSF major causative factor of betel nut chewing. The main pathogenesis is oral submucous connective tissue layer produced more collagen and collagen breakdown decreased, leading to excessive accumulation of collagen. Microvascular is also reduced due to excessive accumulation of collagen, thereby reducing microvascular cells may lead to reduction of oxygen, fibroblasts in the oral submucous connective tissue layer was in a hypoxic state. Hypoxia can induce hypoxia-inducible factor-1alpha. Recent studies have found that, the expression of HIF1 $\alpha$  is related with fibrosis. Our previous study also found that hypoxia can induce increased expression of collagen. In addition, we found that curcumin can reduce the expression of connective tissue growth factor (CTGF), reduce the expression of the collagen. Curcumin can affect the expression of HIF1 $\alpha$  and affecting fibroblast collagen expression.



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Head and neck cancer is a major health problem throughout the world. In Taiwan, there were 6560 new cases and 2468 cases deaths. The standard of care for HNSCC includes surgery, chemotherapeutic drugs and radiotherapy. 5-year survival rate of advance stage HNSCC remained in the range 32-53% Difficult to treat because variable natural behavior of the cancer. Local invasion and frequent regional lymph node metastasis, together with relative resistance to chemotherapeutic drugs. Despite increased experience in surgical technology and adjuvant treatment, the overall prognoses of HNSCC remain unimproved. Need of a novel strategy for HNSCC treatment.

Cancer stem cells are functionally defined as a subset of tumor cells that exhibit the ability of self-renewal and multipotency, serving as progenitor cancer cells.

Sphere (CSC) were more resistant than the parental cell when using the combined treatment(CCRT) A small population of cancer stem cells.

The isolation of CSCs from cancer cells: based on the expression of specific cell surface markers, such as CD133, CD44 and ALDH.

CSC isolation of chemotherapeutic-drug-resistant cell can provide a limited number of CSCs(20-40%)

Concurrent studies confirmed that the sphere culture system are culture in serum-free medium supplemented with adequate mitogens, such as fibroblast growth factor(bFGF) and epidermal growth factor (EGF)

Head and neck cancer tumor initiating cells have been known to have the capacity to promote tumor progression and metastasis and also contribute to radioresistance and chemoresistance.

ALDH+ cells from HNSCC cell lines showed enhanced invasion, a phenotype consistent with EMT and spheroid formation.

Upregulation of snail, twist, alpha-SMA and vimentin and downregulation of E-cadherin.

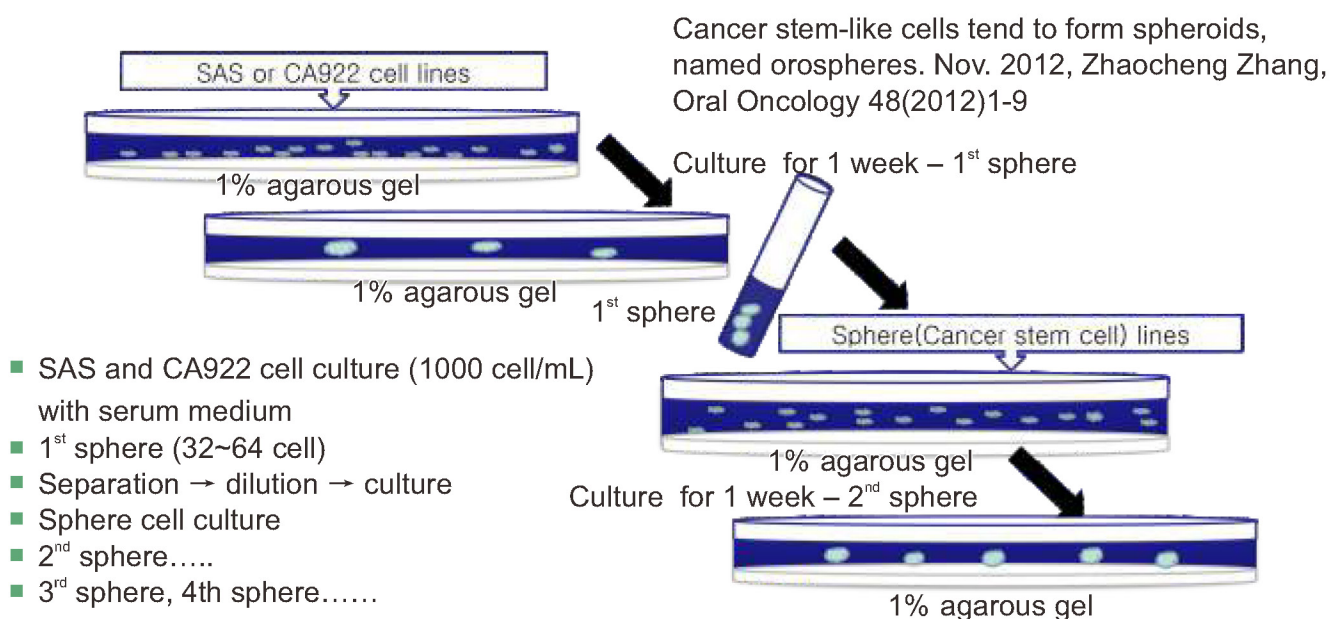
EMT may ultimately contribute to local invasion and metastatic spread frequently observed in patients with head and neck cancer.

## Materials & Methods

Aim 1: Establish cancer stem cells culture system as a model of rapid and adequate sphere formation

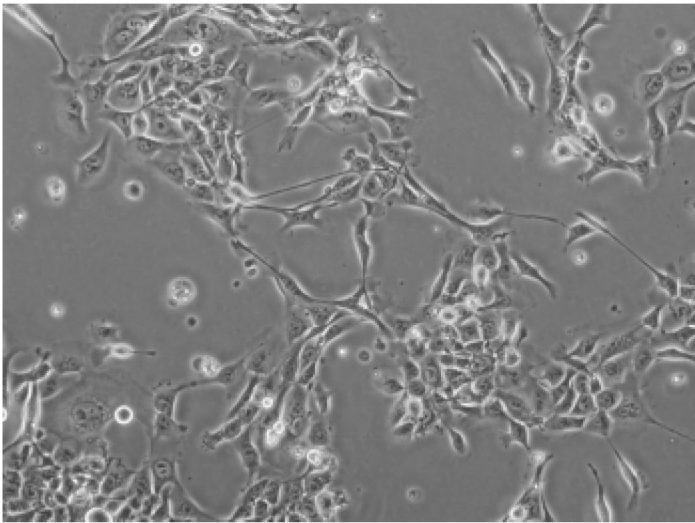
Aim 2: Prove the spheres expressed putative stem cell markers

Aim 3: Clinical drug targets cancer stem cells therapy



## Results

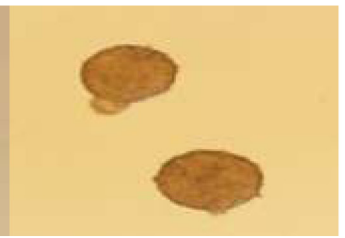
SAS cell lines attached to dish



Sphere 1<sup>st</sup> day



Sphere 4<sup>th</sup> day

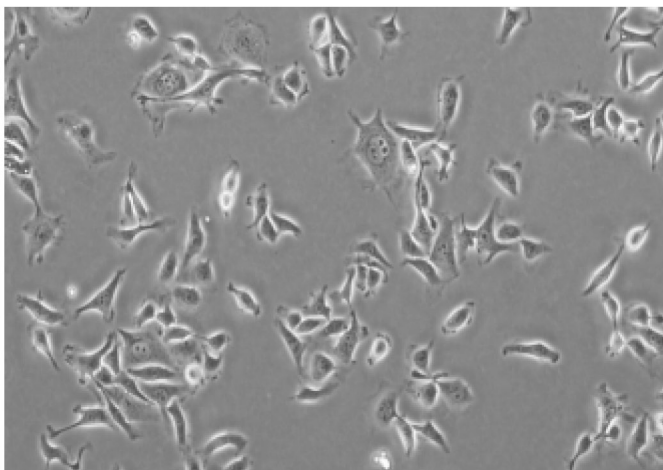


Sphere 6<sup>th</sup> day

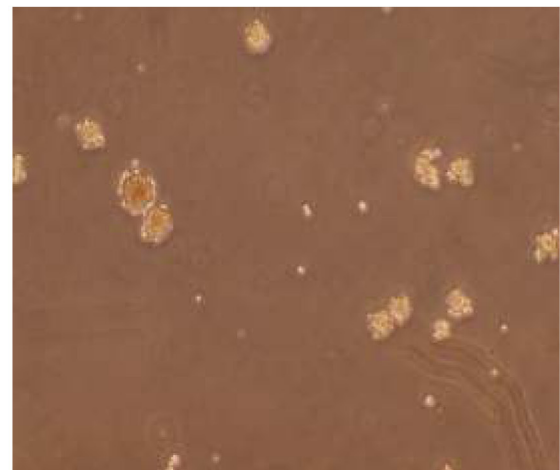


Picture and lab data from steven Ya

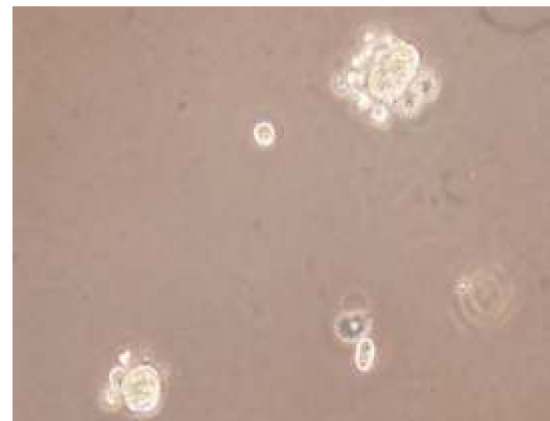
CA922 cell lines attached to dish



Sphere 4<sup>th</sup> day



Sphere 4<sup>th</sup> day



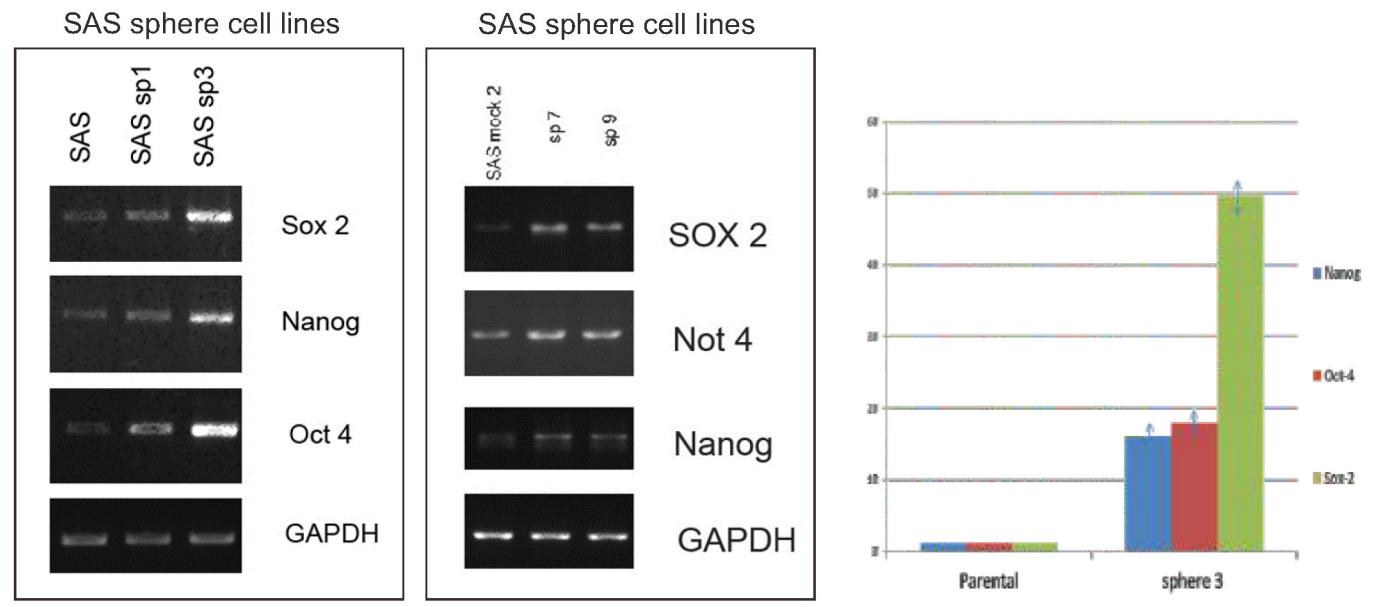
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Prove the spheres expressed putative stem cell markers  
Increased expression in tumor spheres

OCT4 Sox 2 Nanog Lin28 CD44 CD133 Aldehyde dehydrogenase (ALDH).

Comparison of the expression of CSC markers between SAS parental cells and SAS spheres



Picture and lab data from Steven Ya

CSC isolation of chemotherapeutic-drug-resistant cell can provide a limited number of CSCs(20-40%) → Production of larger number of CSCs was expensive and time consuming.

Recent studies: CSCs can be enriched in spheres when cultured in serum-free medium supplemented with adequate growth factors. long time consuming, and cost-ineffective. We culture the CSC with serum medium without growth factors; Established Rapid and adequate sphere formation

### Discussion & Concussion

Quercetin in elimination of tumor initiating stem-like and mesenchymal transformation property in head and neck cancer Enhanced the inhibition of self-renewal, stemness markers, and migration capability in HNSCC. Conclusion: HNC TICs characteristics may therefore be valuable therapeutics clinically in combination with standard treatment modalities.

Curcumin A natural product with low toxic and anti-cancer property  
FDA approved safe food additive and Potential candidate  
Directly interacting with its target proteins or regulating the expression of target genes.  
Anti-oxidant, antimicrobial, anti-inflammatory activities and anti-cancer property Safe at doses of 8 g/d Inhibited proliferation, migration, invasion and metastasis  
Induced apoptosis via modulating multiple signaling pathways  
Curcumin regulated multiple signaling pathways, underlying mechanisms still remain

unclear. Several clinical trials of curcumin are ongoing in HNC, but the anti-cancer activity has not been reported yet. Does curcumin abrogate invasiveness tumorigenicity of head and neck cancer-derived spheres? Are down regulation of mesenchymal transformation markers in head and neck cancer –derived sphere by curcumin? Other drugs: SAHA, EGCG, other inhibitor for therapy. CSCs: self-renewal, invasion, migration and chemotherapeutic-drug-resistance Reduction chemotherapeutic-drug-resistance, Reduction tumor local recurrence rate and metastasis rate. Increase the survival rate and reduction the mortality. Investigate the therapeutic effect and molecular mechanisms of curcumin on cancer stem cell

## Reference

1. Primo, F.L., et al., *Magnetic nanoemulsions as drug delivery system for Foscan®: Skin permeation and retention in vitro assays for topical application in photodynamic therapy (PDT) of skin cancer*. Journal of Magnetism and Magnetic Materials, 2007. 311(1): p. 354-357.
2. Braathen, L.R., et al., *Guidelines on the use of photodynamic therapy for nonmelanoma skin cancer: an international consensus*. Journal of the American Academy of Dermatology, 2007. 56(1): p. 125-143.
3. Shafirstein, G., et al., *Using 5-aminolevulinic acid and pulsed dye laser for photodynamic treatment of oral leukoplakia*. Archives of Otolaryngology–Head & Neck Surgery, 2011. 137(11): p. 1117-1123.
4. Chen, H.-M., et al., *Successful treatment of oral verrucous hyperplasia with topical 5-aminolevulinic acid-mediated photodynamic therapy*. Oral oncology, 2004. 40(6): p. 630-637.
5. Yu, C.-H., et al., *Photodynamic therapy outcome for oral verrucous hyperplasia depends on the clinical appearance, size, color, epithelial dysplasia, and surface keratin thickness of the lesion*. Oral oncology, 2008. 44(6): p. 595-600. .
6. Castano, A.P., T.N. Demidova, and M.R. Hamblin, *Mechanisms in photodynamic therapy: part one—photosensitizers, photochemistry and cellular localization*. Photodiagnosis and photodynamic therapy, 2004. 1(4): p. 279-293.
7. Wu, R., et al., *Photodynamic effects on nasopharyngeal carcinoma (NPC) cells with 5-aminolevulinic acid or its hexyl ester*. Cancer letters, 2006. 242(1): p. 112-119



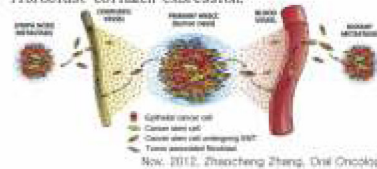
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Head and neck cancer is a major health problem throughout the world. In Taiwan, there were 6560 new cases and 2408 cases deaths. The standard of care for HNSCC includes surgery, chemotherapeutic drugs and radiotherapy. 5-year survival rate of advance stage HNSCC remained in the range 32-53%. Difficult to treat because variable natural behavior of the cancer. Local invasion and frequent regional lymph node metastasis, together with relative resistance to chemotherapeutic drugs. Despite increased experience in surgical technology and adjuvant treatment, the overall prognosis of HNSCC remain unimproved. Need of a novel strategy for HNSCC treatment.

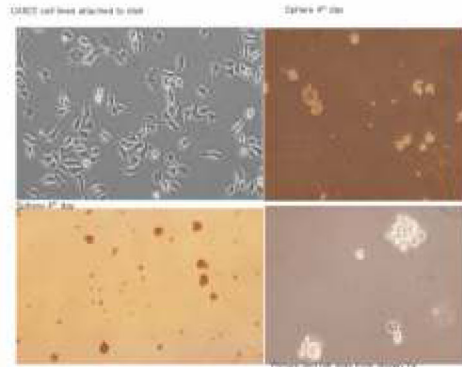
Cancer stem cells are functionally defined as a subset of tumor cells that exhibit the ability of self-renewal and multipotency, serving as progenitor cancer cells. Sphere (CSC) were more resistant than the parental cell when using the combined treatment(DCKT). A small population of cancer stem cells. The isolation of CSCs from cancer cells: based on the expression of specific cell surface markers, such as CD133, CD44 and ALDH1. CSC isolation of chemotherapeutic-drug-resistant cell can provide a limited number of CSCs(20-40%). Concurrent studies confirmed that the sphere cultures system are culture in serum-free medium supplemented with adequate mitogens, such as fibroblast growth factor(FGF) and epidermal growth factor (EGF). Head and neck cancer tumor initiating cells have been known to have the capacity to promote tumor progression and metastasis and also contribute to radioresistance and chemoresistance. ALDH1+ cells from HNSCC cell lines showed enhanced invasion, a phenotype consistent with EMT and spheroid formation. Upregulation of snail, twist, alpha-SMA and vimentin and downregulation of E-cadherin. EMT may ultimately contribute to local invasion and metastatic spread frequently observed in patients with head and neck cancer.

Materials & Methods

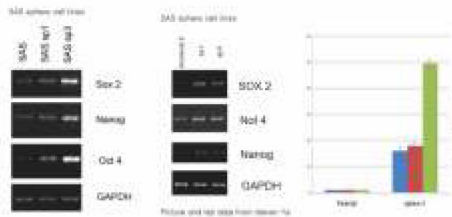
- Aim 1: Establish cancer stem cells culture system as a model of rapid and adequate sphere formation
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Results



Prove the spheres expressed putative stem cell markers  
Increased expression in tumor spheres  
Oct4 Sox 2 Nanog Lin28 CD44 CD133 Aldehyde dehydrogenase (ALDH1). Comparison of the expression of CSC markers between SAS parental cells and SAS spheres



CSC isolation of chemotherapeutic-drug-resistant cell can provide a limited number of CSCs(20-40%) → Production of larger number of CSCs was expensive and time consuming. Recent studies: CSCs can be enriched in spheres when cultured in serum-free medium supplemented with adequate growth factors, long time consuming, and cost-ineffective. We culture the CSC with serum medium without growth factors: Established Rapid and adequate sphere formation

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Quercetin in elimination of tumor initiating stem-like and mesenchymal transformation property in head and neck cancer Enhanced the inhibition of self-renewal, stemness markers, and migration capability in HNSCC. Conclusion: HNC TICs characteristics may therefore be valuable therapeutics clinically in combination with standard treatment modalities. Curcumin natural product with low toxic and anti-cancer property FDA approved safe food additive and Potential candidate Directly interacting with its target proteins or regulating the expression of target genes. Anti-oxidant, antimicrobial, anti-inflammatory activities and anti-cancer property Safe at doses of 8 g/d Inhibited proliferation, migration, invasion and metastasis Induced apoptosis via modulating multiple signaling pathways Curcumin regulated multiple signaling pathways, underlying mechanisms still remain unclear. Several clinical trials of curcumin are ongoing in HNC, but the anti-cancer activity has not been reported yet. Does curcumin abrogate invasiveness tumorigenicity of head and neck cancer-derived spheres? Are down regulation of mesenchymal transformation markers in head and neck cancer - derived sphere by curcumin? Other drugs: SB41, EGCG, other inhibitor for therapy. CSCs: self-renewal, invasion, migration and chemotherapeutic-drug-resistance Reduction chemotherapeutic-drug-resistance, Reduction tumor local recurrence rate and metastasis rate. Increase the survival rate and reduction the mortality. Investigate the therapeutic effect and molecular mechanisms of curcumin on cancer stem cell

Reference

1. Wang, G., et al., Molecular characterization of drug delivery system for Curcumin: Molecular characterization and synthesis of polymeric nanoparticles for oral cancer therapy. *Journal of Molecular and Microbiology*, 2007, 64(1): p. 134-137.
2. Wroblewski, L.E., et al., Evaluation of the use of photodynamic therapy for endometrial carcinoma: an international consensus. *Journal of the American Academy of Dermatology*, 2001, 45(1): p. 12-14.
3. Hattori, H., et al., Topical photodynamic and photothermal laser for photoacoustic treatment of oral leukoplakia. *Archives of Otolaryngology-Head & Neck Surgery*, 2011, 137(10): p. 1177-1181.
4. Chen, H.M., et al., The useful treatment of oral carcinoma. *Journal of Clinical Investigation and Research*, 2011, 4(4): p. 056-057.
5. Yu, C.H., et al., Photodynamic therapy combined with curcumin for oral carcinoma: apoptosis depends on the critical gene p53, c-myc, and cyclin D1, and further down regulation of the tumor. *Journal of Molecular Biology*, 2006, 446(1): p. 395-405.
6. Larkin, J.P., et al., Osimertinib and M.K. Rashkin, Molecularly targeted therapy post other chemotherapeutics. *Advances in Cancer Treatment*, 2014, 2(4): p. 176-191.
7. Kim, S., et al., Photodynamic therapy on squamous carcinoma (SCC) cells with Curcumin. *Journal of In Vitro Fertilization*, 2006, 34(1): p. 111-116.

## 第25屆大會壁報論文比賽 診所組 第一名



### 藉數位流程及黏著式陶瓷膺復體

### 治療兒童牙釉質發育缺陷的恆齒—病例報告

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1.品安牙醫診所；2.振興醫院牙科部；3.國防醫學院牙醫學系；4.高雄醫學院口衛系

#### 摘要

牙釉質發育缺陷(Developmental Defects of Enamel, DDE)是兒童牙科常見的問題，DDE的牙齒容易在萌發後因咬合力造成牙釉質破裂(Posteruptive Enamel Breakdown, PEB)，伴隨蛀牙而形成大範圍的破壞，此時必須使用不銹鋼牙套及鑄造金屬冠來治療。然而，隨著微創牙醫學的發展及材料的進步，黏著式陶瓷膺復體(Bonded Porcelain/ Partial Restoration, BPR)可以保留更多結構、並且存活率與顏色穩定性都較樹脂填補效果佳。同時，藉由數位流程的輔助，我們可以更快速、更舒適的完成複雜治療。本文共提出三例DDE併發PEB兒童患者病例報告，結果顯示在數位流程輔助下，孩童可以在最短時間完成BPR的療程，並有良好的追蹤結果。

#### 前言

DDE是牙釉質在形成過程中，因為牙釉質器官受到干擾或是破壞，造成牙釉質在品質或是數量的變化[1]，可能會讓牙釉質產生窩洞、紋路、變薄甚至消失，或是因礦化不全而產生透明與不透明缺陷。缺陷依外型可分為擴散型與限定型；依顏色可分為白色、黃色與棕色[2]。DDE的牙齒，也容易在患部因咬合力PEB[3]，PEB發生後，會因不易清潔而形成蛀牙，進而造成更大範圍的破壞。當破壞範圍過大，便造成不易填補或是填補物維持效果不佳，此時，不銹鋼牙套及鑄造金屬冠便成為治療的主要方式。

DDE在乳牙齒列的盛行率為30%-70%、恆牙齒列的盛行率為9%-68%[4]，最常發生的型態是限定型不透明缺陷，而且出生體重越輕越容易發生[1]。最常發生的牙位是#12，最少發生的牙位是#14[5]。同時，發生在恆牙第一大臼齒與門牙的DDE，因其特殊性而給予另一個診斷：臼齒-門牙礦化不全症(Molar incisor hypomineralization, MIH)。DDE發生的原因，多數認為是多重因素造成，初步將可能的原因分成[4]：

- 一、全身性：
  - 1.遺傳因素(inherited)：如遺傳性疾病Amelogenesis imperfecta。
  - 2.後天情況(acquired conditions)：產前、圍產期及產後三種時期中產生的問題。
  - 3.環境因素：化學物質與藥物。

二、局部性：感染、外傷、放射線。

DDE的牙齒，除影響美觀外，發生蛀牙的機率是正常牙的4.2倍[6]。而DDE的牙齒也有可能在進食或刷牙時會產生敏感與疼痛。PEB發生後，可能造成牙齒急遽破壞、增加疼痛風險。DDE的完整治療，除針對牙齒的問題外，也必須要注意口腔衛生保健以及飲食諮詢。

為了保留更多的牙齒結構，同時也能兼顧穩定與高存活率，我們嘗試使用BPR來取代不銹鋼牙套。同時，藉由數位流程，來協助患者在較舒適且較少的約診次數下完成治療。本次報告提出三個病例，三位都是DDE併發PEB與蛀牙的孩童患者，並都在數位流程下完成BPR治療。

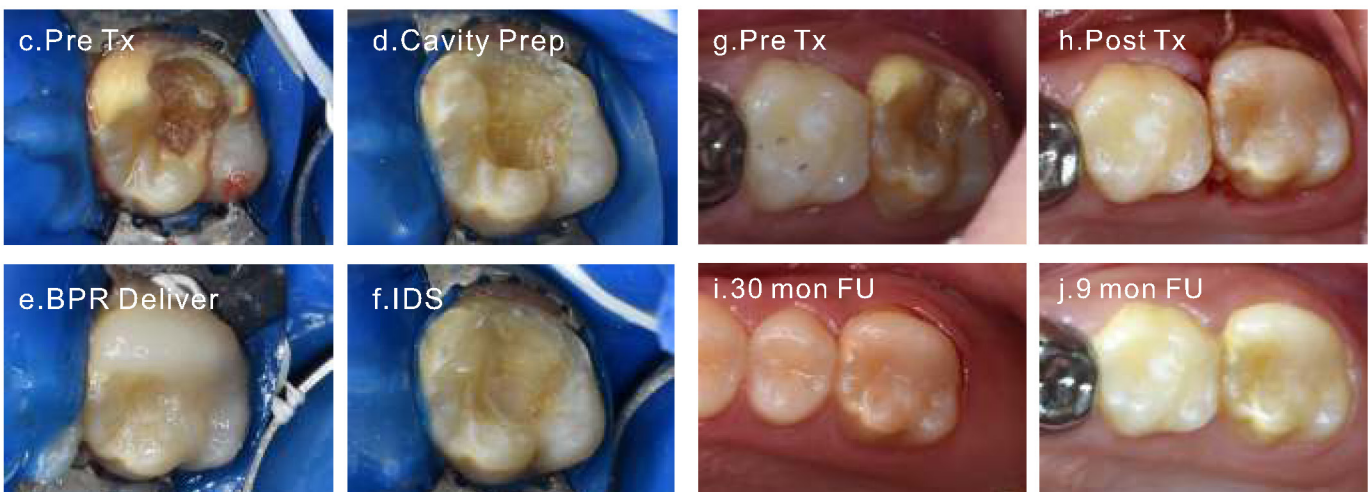
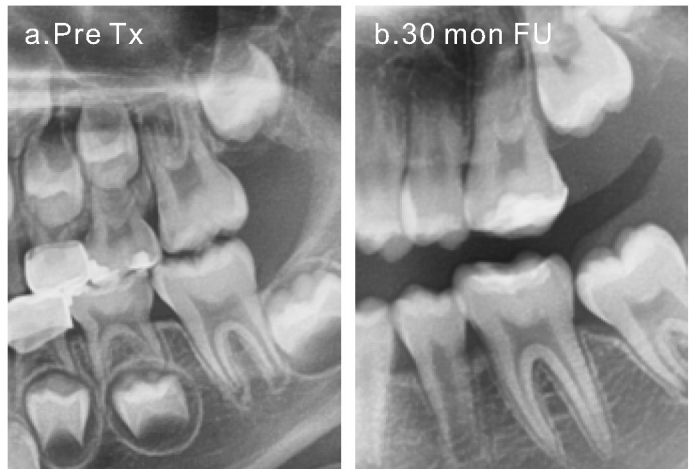
## 病例

### 病例一

年紀：7yr9mon，男

治療過程：

1. #26 DDE with PEB and caries，經討論同意後進行BPR復形。
2. 經局部麻醉、橡皮帳放置後，進行窩洞製備，即時牙本質封閉(immediate dentin sealing, IDS)，並利用數位流程，進行BPR (Lava, 3M)復形。
3. 分別於術後第4月、9月、24月與30月回診，追蹤檢查發現外觀完整顏色保持良好。

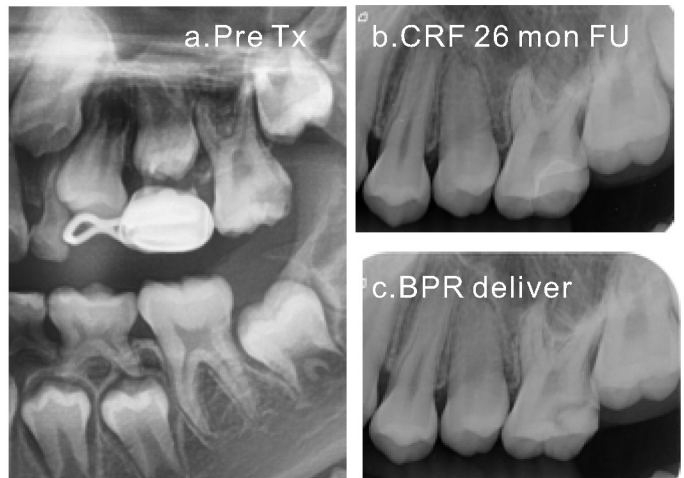


## 病例二

年紀：11yr3mon，女

治療過程：

- 1.門診檢查發現#26 DDE with PEB and caries(圖a,d)，經討論後進行Dycal liner與樹脂填補(圖 e,f,g)。
- 2.樹脂填補後第26月回診復查，發現填補物邊緣破損(圖b,h)，經討論同意後進行BPR 復形。
- 3.經局部麻醉，進行窩洞製備、IDS，並利用數位製程進行BPR(E.max, Ivoclar)復形(圖l,j,k,c)。



## 病例三

年紀：7yr7mon，女

治療過程：

- 1.門診檢查發現#14 DDE with PEB and caries，經討論同意後進行BPR 復形。
- 2.經局部麻醉，進行窩洞製備，IDS，並利用數位流程進行BPR(Lava, 3M)復形。



## 討論

Dhareula [7]針對MIH孩童進行間接樹脂嵌體復形，經過34.8個月追蹤，發現嵌體可以完全去除治療前的敏感、同時邊緣及型態的完整性依然維持良好。Naik [8]研究BPR不同材料的存活率，發現第五年存活率玻璃陶瓷(92%)>長石陶瓷(90%)>樹脂(86%)，第十年存活率長石陶瓷(91%)>玻璃陶瓷(89%)>樹脂(75%)。BPR的存活率與牙齒位置無關，而常見失敗原因依序為斷裂(6.2%)、根管問題(3%)、二度蛀牙(1.7%)以及鷹復體鬆脫(0.9%)。同時，樹脂斷裂的失敗率為10%，遠高於陶瓷斷裂的5.9%。

即時牙本質封閉(IDS)[9]，是取模前先在牙本質塗上牙本質黏著劑，用來增加黏著強度、減少縫隙形成、減少細菌滲漏以及降低牙本質敏感。同時合併使用流動樹脂來做為低彈性係數的底墊，可以保留更多牙齒結構及增加BPR長期存活率。

Ayres [10]比較數位流程與傳統流程，發現兩者在準確性、貼合度以及臨床表現上並無顯著差異。Bandiaky [11]分析口內數位取模以及傳統取模兩者的差異，認為兩者在臨床操作所需時間以及邊緣密合度並無統計差異，但口內數位掃描會讓患者感受較舒適。

本次三個兒童病例都是DDE合併PEB，在數位流程下經IDS處理後裝置PBR。其中病例二的先經過直接樹脂填補，但在術後第26個月因為邊緣破損而必須重新處理。對於兒童牙科的患者來說，利用口內數位取模並結合診間端設計及製造(Chairside CAD/CAM)，可以讓患者保留最多牙齒結構，並可在單一診次中，用較舒適的方式來完成BPR的療程，相信這是對患者、家長及醫師三贏的治療方式。

將來會繼續執行更多的病例及持續追蹤所有病歷的長期療效，並詳細記錄臨床及放射線檢診，希望能獲得更多及更佳的成功率。爾後完成學術文章提供給牙醫界參考及改進。

## 結論

相對樹脂填補，BPR更穩定、更美觀以及更持久。數位流程能減少回診及打麻藥的次數，同時沒有傳統取模的不適感，有利於兒童患者的治療。

## 參考文獻

1. Correa-Faria, P., et al., *Developmental defects of enamel in primary teeth: prevalence and associated factors*. Int J Paediatr Dent, 2013. 23(3): p. 173-9.
2. Fabrizio Guerra, M.M., Denise Corridore, Mauro Capocci, Livia Ottolenghi *Developmental Defects of Enamel: an increasing reality in the everyday practice* Senses Sci, 2014. 1(3): p. 87-95.
3. Oliver, K., et al., *Distribution and severity of molar hypomineralisation: trial of a new severity index*. 2014. 24(2): p. 131-51.

4. Bernadette K. Drummond , N.K., Planning and Care for Children and Adolescents with Dental Enamel Defects. 2015.
5. Ravindran, R. and A.M. Saji, *Prevalence of the developmental defects of the enamel in children aged 12-15 years in Kollam district.* J Int Soc Prev Community Dent, 2016. 6(1): p. 28-33.
6. Andrew Pierce, J.Z., Allison Levans, Robert J Schroth, *The association between developmental defects of enamel and early childhood caries in American Indian children: a retrospective chart review.* Pediatric dentistry, 2020. 15;42(2):126-131.
7. Dhareula, A., et al., *Esthetic rehabilitation of first permanent molars affected with severe form of Molar Incisor Hypomineralization using indirect composite onlays-A case series.* Pediatric Dental Journal, 2018. 28(2): p. 62-67.
8. Naik, V.B., et al., *Comparative evaluation of clinical performance of ceramic and resin inlays, onlays, and overlays: A systematic review and meta analysis.* J Conserv Dent, 2022. 25(4): p. 347-355.
9. MAGNE, P., *Immediate Dentin Sealing: A Fundamental Procedure for Indirect Bonded Restorations.* Journal of Esthetic and Restorative Dentistry, 2005. Volume 17(Issue 3 ): p. p. 144-154.
10. Ayres, G., et al., *Is the digital workflow more efficient for manufacturing partial-coverage restorations? A systematic review.* J Prosthet Dent, 2023.
11. Bandiaky, O.N., et al., *Comparative assessment of complete-coverage, fixed tooth-supported prostheses fabricated from digital scans or conventional impressions: A systematic review and meta-analysis.* The Journal of Prosthetic Dentistry, 2022. 127(1): p. 71-79.





## 藉數位流程及黏著式陶瓷贗復體治療兒童牙釉質發育缺陷的恆齒—病例報告

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### 摘要

牙釉質發育缺陷(Developmental Defects of Enamel, DDE)是兒童牙科常見的問題，DDE的牙齒容易在萌發後因咬合力造成牙釉質破裂(Posteruptive Enamel Breakdown, PEB)，伴隨蛀牙而形成大範圍的破壞，此時必須使用不銹鋼牙套及鑲造金屬冠來治療。然而，隨著微創牙醫學的發展及材料的進步，黏著式陶瓷贗復體(Bonded Porcelain/Partial Restoration, BPR)可以保留更多結構，並且存活率與顏色穩定性都較樹脂填補效果佳。同時，藉由數位流程的輔助，我們可以更快、更舒適的完成複雜治療。本文共提出三例DDE併發PEB兒童患者病例報告，結果顯示在數位流程輔助下，孩童可以在最短時間完成BPR的療程並有良好的追蹤結果。

### 前言

DDE是牙釉質在形成過程中，因為牙釉質器官受到干擾或是破壞，造成牙釉質在品質或是數量的變化[1]，可能會讓牙釉質產生窩洞、紋路、變薄甚至消失，或是因礦化不全而產生透明與不透明缺陷。缺陷依外型可分為擴散型與限定型；依顏色可分為白色、黃色與棕色[2]。DDE的牙齒，也容易在患部因咬合力PEB[3]，PEB發生後，會因不易清潔而形成蛀牙，進而造成更大範圍的破壞。當破壞範圍過大，便造成不易填補或是填補物維持效果不佳。此時，不銹鋼牙套及鑲造金屬冠便成為治療的主要方式。

DDE在乳牙齒列的盛行率為30%-70%，恆牙齒列的盛行率為9%-68%[4]，最常發生的型態是限定型不透明缺陷，而且出生體重越輕越容易發生[1]，最常發生的牙位是#12，最少發生的牙位是#14[5]。同時，發生在恆牙第一大臼齒與門牙的DDE，因其特殊性而給予另一個診斷：白齒-門牙礦化不全症(Molar incisor hypomineralization, MIH)。DDE發生的原因，多數認為是多重因素造成，初步將可能的原因分成[4]：

- 一、全身性：1.遺傳因素(inherited)：如遺傳性疾病Amelogenesis imperfecta。2.後天情況(acquired conditions)：產前、圍產期及產後三種時期中產生的問題。3.環境因素：化學物質與藥物。
- 二、局部性：感染、外傷、放射線。

DDE的牙齒，除影響美觀外，發生蛀牙的機率是正常牙的4.2倍[6]，而DDE的牙齒也有可能是在進食或刷牙時會產生敏感與疼痛。PEB發生後，可能造成牙齒急遽破壞，增加疼痛風險。DDE的完整治療，除針對牙齒的問題外，也必須要注意口腔衛生保健以及飲食諮詢。

為了保留更多的牙齒結構，同時也能兼顧穩定與高存活率，我們嘗試使用BPR來取代不銹鋼牙套。同時，藉由數位流程，來協助患者在較舒適且較少的約診次數下完成治療。本次報告提出三個病例，三位都是DDE併發PEB與蛀牙的孩童患者，並都在數位流程下完成BPR治療。

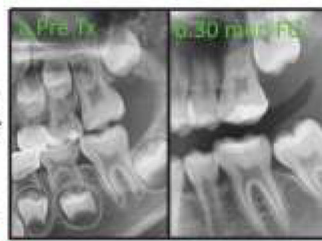
### 病例

#### 病例一

年紀：7yr9mon，男

治療過程：

1. #26 DDE with PEB and caries，經討論同意後進行BPR復形。
2. 經局部麻醉，橡皮障放置後，進行窩洞製備，即時牙本質封閉(immediate dentin sealing, IDS)，並利用數位流程，進行BPR (Lava, 3M)復形。
3. 分別於術後第4月、9月、24月與30月回診，追蹤檢查發現外觀完整顏色保持良好。

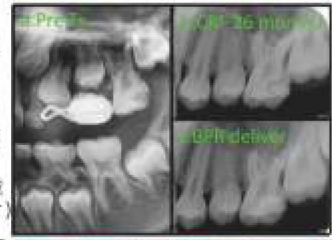


#### 病例二

年紀：11yr3mon，女

治療過程：

1. 門診檢查發現#26 DDE with PEB and caries(圖a,d)，經討論後進行Dycal liner與樹脂填補(圖e,f,g)。
2. 樹脂填補後第26個月回診復查，發現填補物邊緣破損(圖b,h)，經討論同意後進行BPR復形。
3. 經局部麻醉，進行窩洞製備，IDS，並利用數位製程進行BPR(E.max, Ivoclar)復形(圖i,k,c)。



#### 病例三

年紀：7yr7mon，女

治療過程：

1. 門診檢查發現#14 DDE with PEB and caries，經討論同意後進行BPR復形。
2. 經局部麻醉，進行窩洞製備，IDS，並利用數位製程進行BPR(Lava, 3M)復形。



### 討論

Dhareula [7]針對MIH孩童進行間接樹脂嵌體復形，經過34.8個月追蹤，發現嵌體可以完全去除治療前的敏感，同時邊緣及型態的完整性依然維持良好。Naik [8]研究BPR不同材料的存活率，發現第五年存活率玻璃陶瓷(92%)>長石陶瓷(90%)>樹脂(86%)，第十年存活率長石陶瓷(91%)>玻璃陶瓷(89%)>樹脂(75%)。BPR的存活率與牙齒位置無關，而常見失敗原因依序為斷裂(6.2%)、根管問題(3%)、二度蛀牙(1.7%)以及廣度體鬆脫(0.9%)。同時，樹脂斷裂的失敗率為10%，遠高於陶瓷斷裂的5.9%。即時牙本質封閉(IDS)[9]，是取模前先在牙本質塗上牙本質黏著劑，用來增加黏著強度、減少縫隙形成、減少細菌滲漏以及降低牙本質敏感。同時合併使用流動樹脂來做為低彈性係數的底墊，可以保留更多牙齒結構及增加BPR長期存活率。

Ayres [10]比較數位流程與傳統流程，發現兩者在準確性、貼合度以及臨床表現上並無顯著差異。Bandiaky [11]分析口內數位取模以及傳統取模兩者的差異，認為兩者在臨床操作所需時間以及邊緣密合度並無統計差異，但口內數位掃描會讓患者感受較舒適。本次三個兒童病例都是DDE併發PEB，在數位流程下經IDS處理後裝置BPR，其中病例二的先經過直接樹脂填補，但在術後第26個月因為邊緣破損而必須重新處理。對於兒童牙科的患者來說，利用口內數位取模並結合診斷設計及製造(Chairside CAD/CAM)，可以讓患者保留最多牙齒結構，並可在單一診次中，用較舒適的方式來完成BPR的療程，相信這是對患者、家長及醫師三贏的治療方式。將來會繼續執行更多的病例及持續追蹤所有病歷的長期療效，並詳細記錄臨床及放射線檢診，希望能獲得更多及更佳的成功率。爾後完成學術文章提供給牙醫參考及改進。

### 結論

相對樹脂填補，BPR更穩定、更美觀以及更持久。數位流程能減少回診及打麻藥的次數，同時沒有傳統取模的不適感，有利於兒童患者的治療。

### 參考文獻

1. Carrazo-Pardo, R., et al., Developmental defects of enamel in primary teeth: prevalence and associated factors. *Int J Paediatr Dent*, 2018; 23(1): p. 17-9.
2. Fabrizio-Saenz, M.M., Denis-Corcos, M., and Casoli, L., The Oligosaccharide Developmental Defects of Enamel: an increasing entity in the dentin defects index. *ISD*, 2019; p. 47-9.
3. O'Brien, A., et al., Distribution and severity of molar hypomineralization (MIH) of a new severity index. *ISD*, 2012; p. 131-41.
4. Benayahu, K., Eskinovic, N. B., Fleming and Care for Children and Adolescents with Dental Trauma. 2015.
5. Kamalides, K., and Akin, S., Prevalence of the developmental defects of the enamel in children aged 22-33 years in Bulgaria (abstract). *Int Soc Paediatr Community Dent*, 2006; 8(1): p. 38-9.
6. Avila-Ferre, L.S., Wilson Inverso, Robert J. Kennedy, The association between developmental defects of enamel and early childhood caries in American Indian children: retrospective cohort study. *BMC Pediatrics*, 2020; 20:4320-4324-12.
7. Dhareula, K., et al., Aesthetic rehabilitation of first permanent molars affected with severe form of Molar Incisor Hypomineralization using indirect composite inlays: a case report. *Pediatric Dental Journal*, 2018; 26(2): p. 62-67.
8. Naik, V.R., et al., Comparative evaluation of clinical performance of ceramic and resin inlays, onlays, and crowns: A systematic review and meta-analysis. *J Clin Dent*, 2022; 29(4): p. 140-151.
9. Mairor, F., Immediate Dentin Sealing: A Fundamental Procedure for Indirect Restorative Operations. *Journal of the American Academy of Restorative Dentistry*, 2006; Volume 13(2): p. 144-154.
10. Ayres, G., et al., Is the digital workflow more efficient for manufacturing partial coverage restorations? A systematic review. *J Prosthet Dent*, 2021.
11. Bandiaky, C.N., et al., Computerized assessment of complete coverage, final tooth support and preparation (abstract) fabricated from digital scans or conventional impressions: A systematic review and meta-analysis. *The Journal of Prosthetic Dentistry*, 2013; 110(1): p. 71-78.

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