

UNIVERSITI TEKNOLOGI MARA

**ANALYSIS OF PROTEOME
CHANGES IN BONE
REMODELLING INDUCED BY
IMPLANT RETAINED
OVERDENTURES**

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ABSTRACT

Implant-retained overdentures (IRO) have been successful in providing satisfactory treatment for edentulous patients but in most cases, they contribute to bone resorption. The pressure induced by the IRO on the soft tissue mucosa may have mediated proteome changes that lead to this bone resorption. Thus, this study has been carried out to identify the proteome changes associated with bone remodeling induced by IRO. Tissue specimens (n=22) and saliva samples (n=22) were collected from implant-retained overdentures and healthy patients before proteins being extracted and precipitated from the samples. This study employed two-dimensional polyacrylamide gel electrophoresis (2D-PAGE) and matrix-assisted laser desorption-ionization time-of-flight mass spectrophotometry (Maldi-ToF/ToF MS) peptide mass fingerprinting for precise protein identification related to bone remodeling in IRO users. The protein expressions were correlated with the quantified bone resorption by the three-dimensional imaging which was encountered by the IRO wearer. The selection of differentially expressed seven spots based on the ANOVA values ($p \leq 0.05$) and 1.5-fold changes from tissue samples between the subjects (n=11) and the control (n=11) by Progenesis Same Spot software (Nonlinear Dynamics, Durham, NC) was preceded to protein identification by Maldi ToF/ ToF. Through this approach, several proteins were identified: 78 kDa glucose-regulated protein, Serum albumin, Lumican, Ig gamma-1 chain C region, Hemoglobin subunit beta and Heat shock protein beta-1. Among these, three proteins were known involved with bone remodeling based on previous literatures which were 78 kDa glucose-regulated protein, Lumican, and Heat shock protein beta-1. It was found that 78 kDa glucose-regulated protein and Lumican were up-regulated by 2.2-fold ($p= 0.015$) and 1.8-fold ($p= 0.005$) respectively in implant retained overdentures wearers compared to the control group, relating their roles in bone resorption. Meanwhile, Heat shock protein beta-1 was downregulated by 2-fold ($p=0.029$) in IRO group conveying its possible potential roles in the formation of bone. Based on the cellular localization and functions, these proteins' roles could be fitted into the bone remodeling cycle and significantly believed played their parts in the mechanism involved in bone resorption phenomenon associated with IRO.

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CHAPTER ONE

INTRODUCTION

1.1 RESEARCH BACKGROUND

Increased longevity over the decades (Berkey & Berg, 2001; Miniño *et al.*, 2007; Miniño *et al.*, 2006) increases the size of aging population as well as their health care requirements. Toothlessness or edentulism is strongly associated with the elderly population (Natto *et al.*, 2014). The edentulism tendency of the elderly was due to persistent periodontal disease (Axelsson *et al.*, 2004; Shigli K. *et al.*, 2009), low educational level, poor lifestyle and lack of dental care (Thorstensson & Johansson, 2010). Lack of awareness worsens the periodontal disease over time, increasing the level of clinical attachment loss. This resulted in gingival recession followed by bone loss. Tooth then loses its stability and led to tooth loss phenomenon (Natto *et al.*, 2014).

Bone resorption, edentulism and resultant weakening bite force affect efficacy of chewing and reduce facial support, phonetics as well as their self esteem. Eventually, the inferiority complex developed influenced their social life negatively (Geckili *et al.*, 2012). Hence, the quest for denture prosthesis to solve the above mentioned problem has been rising (Salinas, 2009) in proportional with the increasing population of the elderly (Berkey & Berg, 2001; Thomson & Ma, 2014a).

Use of implant-retained overdentures has been successful in providing satisfactory treatment for edentulous patients (Sadowsky *et al.*, 2001). However, prolonged denture wearing may contribute to excessive mechanical and functional pressure which resulted in continuous residual ridge resorption (RRR) underneath the denture (Blum and McCord, 2004; Ahmad *et al.*, 2013). Continuous residual ridge resorption may result in unretentive dentures, pain and discomfort (Huomonen *et al.*, 2012).

The residual ridge resorption has been observed to occur at various degrees of severity. According to previous studies on rat, bone resorption was believed to be triggered by bone disuse atrophy and pressure from denture wear (Sato *et al.*, 1998b).