



# Electron Microscopic Study of Esophageal Epithelium in Non-erosive Reflux Disease

***Yi Yi Myint\*, Dr Ye Tun, Dr Nasser Muhammad Amjad, Dr. Mohd Zailani Hassan, Nor Linda Abd Rashid***

**\*Department of Basic Medical Sciences, Kulliyyah of Medicine, International Islamic University of Malaysia. E-mail:yym\_iiu@hotmail.com**

**Hp: 0129683961**

## Introduction

Non-erosive reflux disease (NERD) is the most common phenotype of gastro-esophageal reflux disease (GERD). Dilated intercellular space (DIS) in prickle cell layer is considered as early signs of acid damage to the esophageal epithelium [1-5].

## Objectives

To explore DIS in both superficial and prickle cell layer of esophageal epithelium of NERD patients and normal controls by using scanning electron microscope (SEM) and transmission electron microscope (TEM).

## Materials and Methods

❖The study group included 8 NERD patients (reflux symptoms, normal mucosa on endoscopy and positive 24-hour pH monitoring) and 5 normal controls.

❖Endoscopic esophageal mucosa biopsies were taken 5 cm proximal to the Z line and specimens were routinely processed for SEM and TEM.

❖The nature of intercellular spaces between superficial cells and prickle cell layers were viewed by SEM and TEM respectively.

## Results: SEM

❖Cellular attachment of superficial cells was divided into 3 grades.

❖It differs significantly among control and NERD patients.  $p$  value was 0.007. (Chi-Square test,  $p < 0.05$  was considered to be statistically significant)

## Results: TEM

Morphometric analysis on TEM microphotographs (Figure 4,5) showed mean intercellular space diameter values of NERD patients were significantly (two times) higher than those in normal controls ( $p < 0.001$ ) in prickle cell layer using student's  $t$ -test. (Table1)

## Results

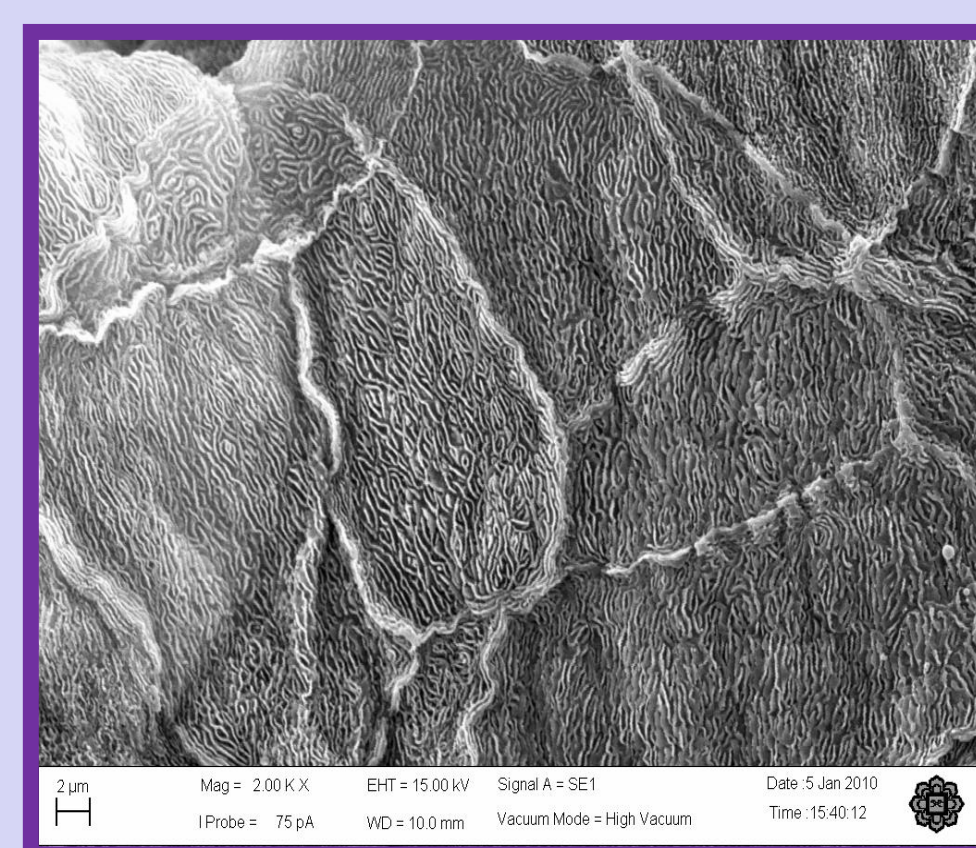


Figure 1- Scanning electron micrograph of esophageal epithelium (Grade1). The superficial cells are closely attached to each other with clear cut cell boundaries. It was detected in 2 out of 5 (40%) controls and non of the NERD subjects.

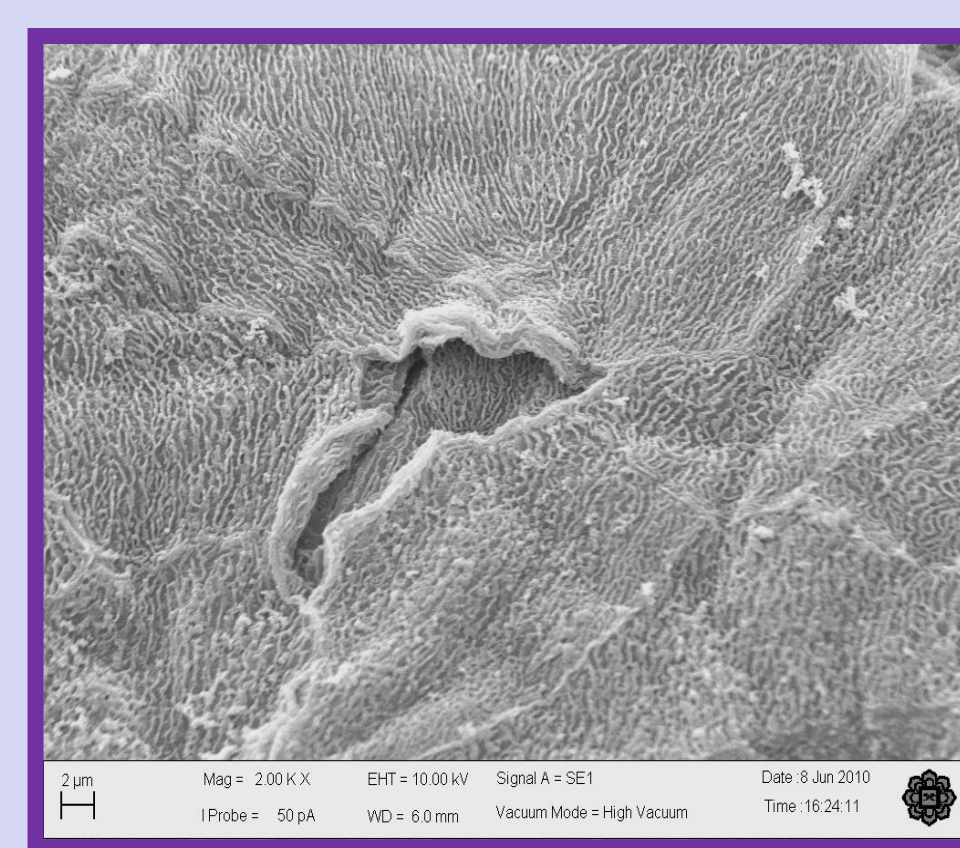


Figure2- Scanning electron micrograph of esophageal epithelium (Grade 2). Cells closely attached but some areas showed widened intercellular spaces. It was found in 1 out of 8 (12.5%) NERD patients and 3 out of 5 (60%) control subjects.

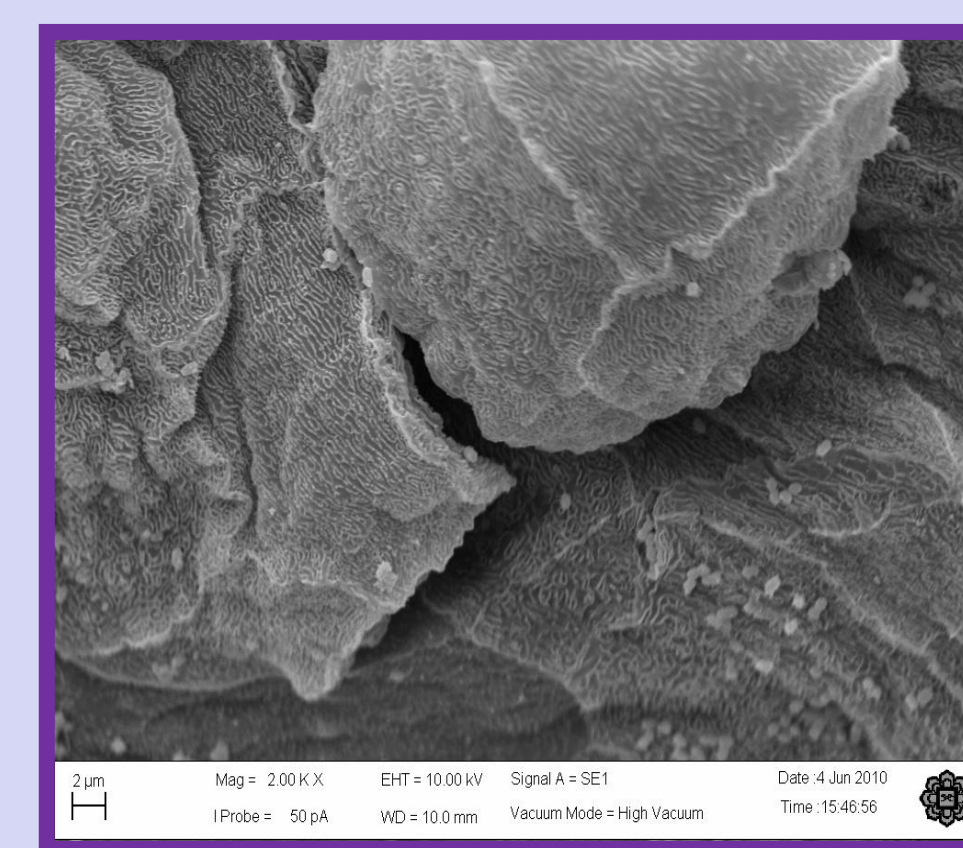


Figure 3- Scanning electron micrograph of superficial esophageal epithelium (Grade 3). Widened intercellular spaces between cells, desquamation and less well developed cell boundaries. It was found in 7 out of 8 (87.5%) NERD and non of the control subjects.

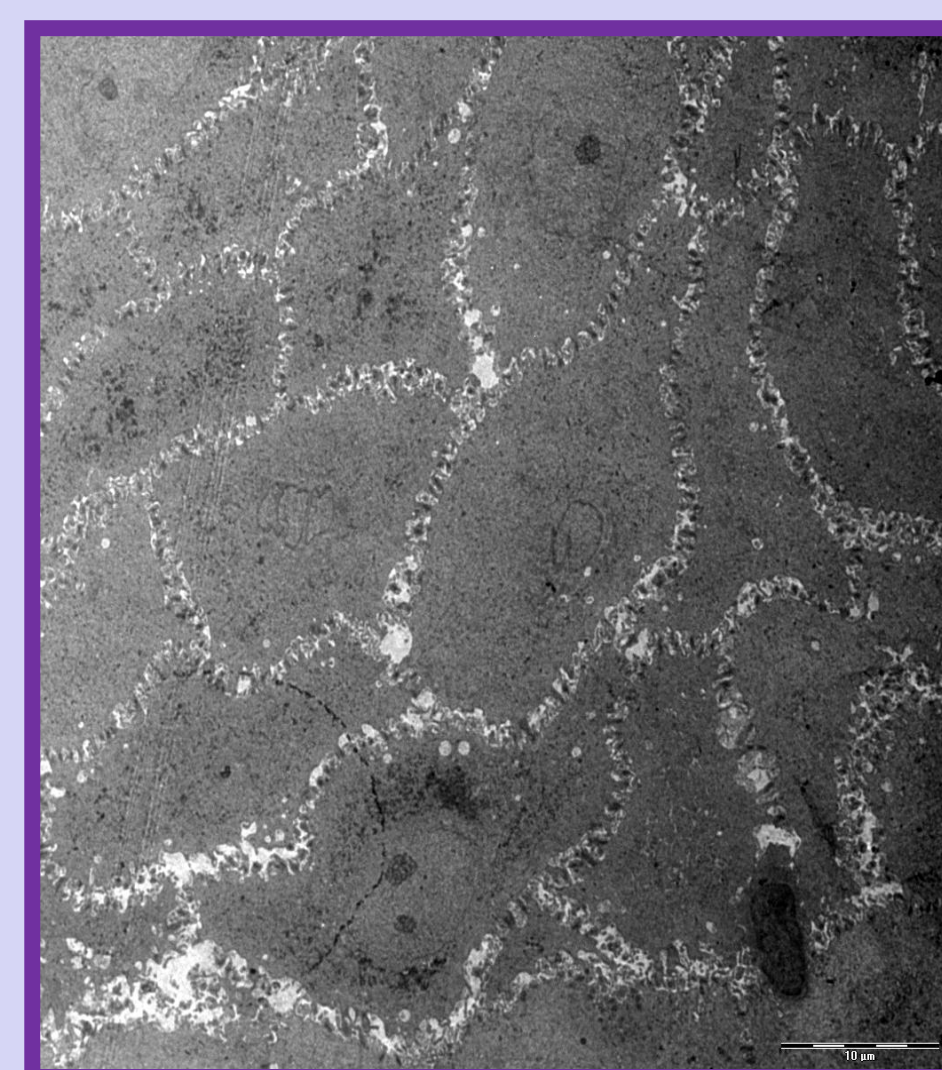


Figure 4: Ultrastructural appearance of prickle cell layer of normal esophageal mucosa in a control subject. (X1000).

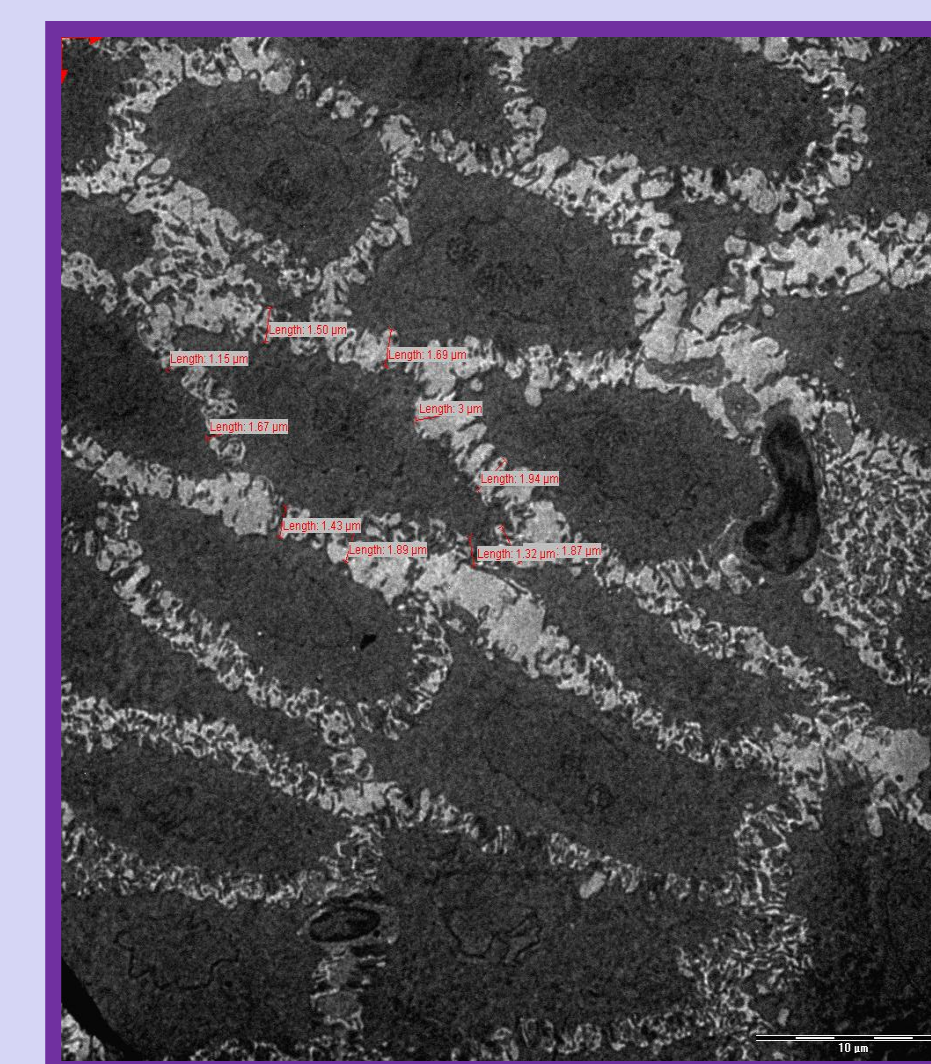


Figure 5. Ultrastructural appearance of prickle cell layer of NERD patient. The intercellular spaces are dilated between the prickle cells. (X1000).

Groups	Intercellular spaces ( $\mu\text{m}$ )		
	Mean	Maximal	Minimal
Control ( n=5)	0.65 ( $\pm$ 0.17)	0.86 ( $\pm$ 0.30)	0.44 ( $\pm$ 0.16)
NERD (n=8)	1.39 ( $\pm$ 0.32)	1.66 ( $\pm$ 0.37)	1.13 ( $\pm$ 0.32)

Table 1 : The intercellular space of 13 subjects.

## Conclusion

❖SEM study on DIS in esophageal surface cells is not a useful diagnostic test for differentiating between normal and NERD patients because at any time, there will be dying and denuded surface cells as part of the normal life cycle of esophageal epithelial cells.

❖TEM study in prickle cell layer is a promising diagnostic finding of early damage of esophageal epithelium in NERD patients

## References

1. Tobey N A, Carson J L, Alkiek R A, Orlando R C. Dilated intercellular spaces: a morphological feature of acid reflux-damaged human esophageal epithelium. *Gastroenterology* 1996; 111 (5): 1200–5.
2. Calabrese C, Fabbri A, Bortolotti M, et al. Dilated intercellular spaces as a marker of esophageal damage: comparative results in gastroesophageal reflux disease with or without bile reflux. *Aliment Pharmacol Ther* 2003;18:525–32
3. Barlow WJ, Orlando RC. The pathogenesis of heartburn in nonerosive reflux disease: a unifying hypothesis. *Gastroenterology* 2005;128:771–8.
4. Caviglia R, Ribolsi M, Maggiano N, et al: Dilated intercellular spaces of esophageal epithelium in nonerosive reflux disease patients with physiological esophageal acid exposure. *Am J Gastroenterol* 2005; 100: 543–548.
5. Xue Y, Zhou L Y, Lin S R. : Dilated intercellular spaces in gastroesophageal reflux disease patients and the changes of intercellular spaces after omeprazole treatment. *Chinese Medical Journal* 2008; 121(14):1297-1301

## Acknowledgements

A special word of gratitude should be dedicated to Research Centre, IIUM for their research grant (EDW B 0905-278 ). Special thanks go to director of HTAA hospital , staffs of endoscopy unit , HTAA, staffs of Endoscopic Suite, Gastrointestinal Laboratory Unit and Electron Microscopy Unit of IIUM .