Variation of the apparent diffusion coefficient measured from various regions of the normal breast tissue using diffusion weighted MRI as a function of various phases of the menstrual cycle.

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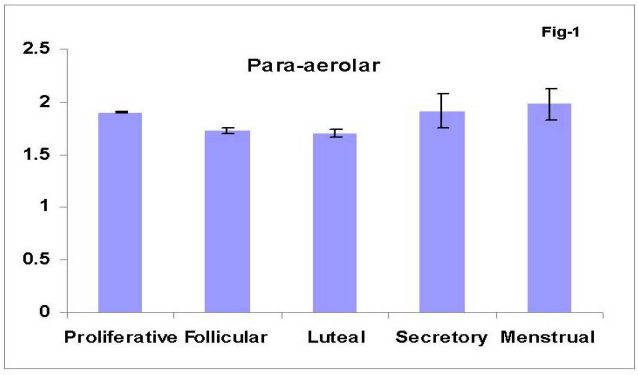
Objective: To evaluate the role of apparent diffusion coefficient (ADC) from various regions of the normal breast tissue of female volunteers as a function of the histological phases of the menstrual cycle

Introduction: It is known that breast tissues show high proliferative activity and histological changes throughout the menstrual cycle (1-3).These changes contribute to the heterogeneity of the breast that may influence the detection of the breast disease. Hence, measurements of water diffusion may dependent on menstrual cycle. ADC values affect both cell density and volume of extracellular matrix. Water inside cells is known to have lower ADC as compared to extracellular water, which is believed to be due to restrictive structural components inside the cell and higher viscosity from increased concentrations of macromolecules. Change in water content or water compartmentalization in the breast during the menstrual cycle may result in an associated change in ADC measured. The aim of this study was to characterize the variability of ADC values of measured in normal women at various phases of their menstrual cycle from various regions of the breast.

Material and methods: A total of nine healthy [average age = 32.2 ± 5.5 (range, 24-42 yrs) years; non-pregnant and non-lactating)], premenopausal female volunteers were included in the study. Eight had regular, approximately 28-30 days menstrual cycle, and one had irregular cycle. None were taking oral contraceptives or had any kind of breast or other diseases which might influence pituitary-ovarian cycling. Written informed consent obtained and Institutional ethical committee approved the study. MR investigations were performed using circularly polarized double breast array coil at 1.5 T (Avanto, Siemens, Germany). DW images were acquired in transverse plane of both the breasts using an EPI with diffusion gradients applied along orthogonal directions concurrently to reduce motion artifacts. The parameters used were: b = 0, 500 and 1000 s/mm^2; TR = 5000 ms; TE= 87 ms; NS = 1, EPI factor =128 and acquisition matrix = 128 x 128; and slice thickness = 5 mm. To study the sequential changes in ADC, the volunteers were scanned sequentially for four weeks [proliferative (days 3-7), follicular (days 8-14), luteal (days 15-20), secretory (21-27), and menstrual phases (days 28-2)]. The ADC values were calculated from four different regions upper and lower quadrants, para-areolar and central region of the breast. One way ANOVA was used to compare the various phases of menstrual cycle. A p-value < 0.05 was considered as significant. All statistical analyses were carried out using statistical software SPSS 11.5.

Results: ADC values for the 4 regions of the breast are shown in Table 1. A ADC value of 1.9 ± 0.01 was observed during the proliferative phase of para-areolar which reduced to 1.73 ± 0.03 and 1.70 ± 0.04 during follicular and luteal phases, respectively. The value increased to 1.91 ± 0.16 during secretory and to 1.98 ± 0.15 during menstrual phases. The ADC value of the para-areolar region was significantly higher during proliferative, secretory and menstrual phases compared to the other regions of the breast as shown in Table 1. The variation of ADC for the para-aerolar region as a function of the menstrual cycle is shown in Fig.1, indicating a cyclic change.

Menstrual	ADC value from different regions of the breast				p-value
	Lower (a)	Upper (b)	Para-areolar (c)	Central (d)	
Proliferative	1.65±0.18	1.63±0.19	1.9±0.01	1.74±0.04	P (b with a, c)
Follicular	1.74±0.20	1.72±0.20	1.73±0.03	1.78±0.17	No significance
Luteal	1.73±0.20	1.71±0.19	1.70±0.04	1.79±0.21	No significance
Secretory	1.74±0.18	1.70±0.18	1.91±0.16	1.83±0.16	P (b with a, c)
Menstrual	1.73±0.17	1.70±0.17	1.98±0..15	1.86±0.15	P (b with a, c)



Discussion: Our study showed that ADC of the para-areolar region was significantly higher during proliferative, secretory and menstrual phases compared to the various regions of the breast. It is known that normal physiological and the histological changes occur in breast tissue throughout the menstrual cycle. The ADC for the upper, lower and central quadrants showed insignificant changes during the menstrual cycle. This indicates that the hormone-associated changes due to menstrual cycle have little effect on ADC in the upper, lower and central quadrants of the breast. It is known that most changes in the breast due to menstrual cycle occur in the fibro glandular tissues (5,6). Thus the para-areolar region which is dominated by glandular tissues showed changes in ADC as a function of the menstrual cycle. Partridge et al have reported variation in ADC measured in the normal breast as a function of menstrual cycle (4). They reported that females with regular menstrual cycle showed no significant influence on ADC except that it decreased during the second week and increased during the fourth week, but statistically insignificant. Our study differs from theirs in that 4 different regions of the breast were monitored sequentially at 5 different phases. In conclusion, our data showed that changes in the normal breast tissue characteristics occur due to physiological factors like menstrual cycle that strongly influence the ADC value especially the para-areolar region in a cyclic manner. Thus, any assessment of breast pathology using ADC values should be carried out carefully taking into consideration the location of tumor within the breast as well as the phases of menstrual cycle.

References: (1)Vogel PM *et al. Am J Pathol* 1981;104: 23-34; (2)Longacre TA *et al . Am J Surg Pathol* 1986; 10: 382-93 ;(3)Potten CS *et al. Br J Cancer*. 1988; 58: 163-70 ;(4).Partridge SC *et al. J Magn Reson Imaging* 2001; 14: 433-438 ; (5).Dean KI *et al. Acta Radiol* 1994; 35: 258-261.(6).Fowler PA *et al. Br J Obstet Gynaecol* 1990; 97: 595-602.