Proven Intra and Interobserver Reliability in the Echographic Assessments of Body Fat Changes Related to HIV Associated Adipose Redistribution Syndrome (HARS)

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Abstract: *Objective*: To prove intra- and inter-observer's reliability of ultrasound (US) in the assessment of lipoatrophic findings related to the HIV associated Adipose Redistribution Syndrome (HARS).

Patients and Methods: In two separated sessions, 2 consecutive measurements of subcutaneous fat thickness (SFT) were performed by each observer at the deepest point of Bichat pad, the dorsal face of arm and the mid thigh for the assessment of facial, brachial and crural lipoatrophy, respectively. We enrolled 20 HIV patients, rotating an experienced and untrained sonologist. The assessments were performed avoiding any stand off pads in the skin and excluding artefacts due to the too abundant quantity of gel to obtaining, with minimal transducer pressure, the best resolution of the reference points.

Results: Means of facial, brachial and crural SFT showed no significant differences between the workers. Coefficients of variability (SD/mean x100) were similar for facial (ranges: 4.7-5.2% *vs* 4.9-5.6%, respectively*)*, brachial (ranges: 5.8-8.4% *vs* 9.7-11.2%) and crural SFTs (ranges: 5.9-6% *vs* 6.2-8.7%). There was greater consistency in the measurements performed by the experienced *vs* the untrained worker. Inter-observer agreement, assessed through kappa statistic (k) analysis, confirmed increased measurement's agreement in the facial (k ranged from 0.40 to 0.60), brachial (k: 0.23-0.63) and crural SFT assessments (k: 0.58-0.70) from the 1st to 2nd session.

Conclusions: US shows low intra observer variability and good inter observer reliability in the assessment of body fat changes related to the HARS. The different degree of consistency by the workers and the improvement of interobserver agreement, suggest to stating a well defined period of training to obtain better US reliability.

Keywords: Sonography, Lipodystrophy, intra and inter-observer reliability, antiretrovirals, body fat changes.

We read the interesting report by Padilla *et al*. [1] about the use of ultrasound (US) in assessing of body fat changes (BFCs) related to HIV associated Adipose Redistribution Syndrome (HARS) [2, 3].

The authors confirm the good accuracy of US [4-10], further validating our opinion that the routine US assessment of related to antiretroviral (ARV) therapy should be part of the standardized procedures in the care of HIV patients. However, some open questions stay on:

1) Computed tomography (CT) is the gold standard tool for the BFCs assessments based on its low variability and high accuracy [11, 12]. Anyhow, recent reports [4-10] have demonstrated the utility of alternative methods such as US, that are easier to perform and more readily available both of which are valuable assets when close follow up is required.

   During the 12th Conference on Retroviruses and Opportunistic Infections, i.e., Moyle *et al*. reported the ability of US to document the recovery of malar subcutaneous fat thickness (SFT) at deepest point of Bichat pad in patients who had been switched to less invaliding new generation of ARVs, using 6 months re-assessments which are not readily feasible with CT.

2) Interestingly, in the few studies that have compared US with CT in measuring SFT [1, 13] the methods proved comparable; however the authors obtained controversial results when assessing malar SFT at the deepest point of Bichat pad [1]. We feel that the question of measurement's technique is crucial to explain these results. Based on our measurement's technique, i.e., our data suggest high comparability between the CT and US measurements of SFT at reference points (RPs) representative of facial, brachial and crural lipoatrophy (LA) (Fig. **1a-c**) [14].

3) Proven, reliable and well standardized RPs have been validated for brachial and crural LA [9], as well as confirmed also by Padilla *et al*. [1]. The RP for facial LA is more controversial.

   In previous reports [8] we observed that US scannings of deepest point of Bichat's pad provide reliable evidence for diagnosing of facial SAT loss (Fig. **1a**). In our investigation we are observing good accuracy of

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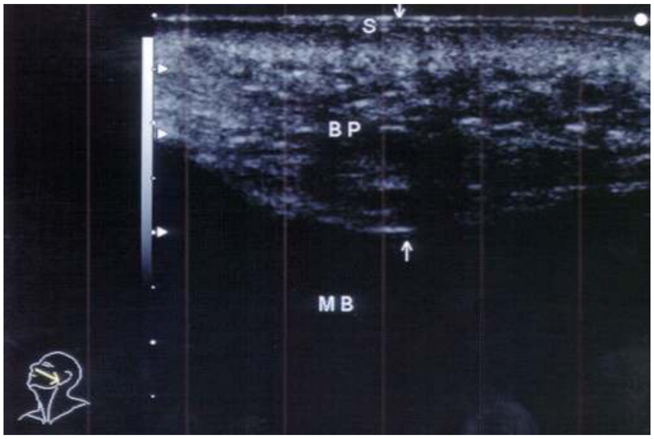
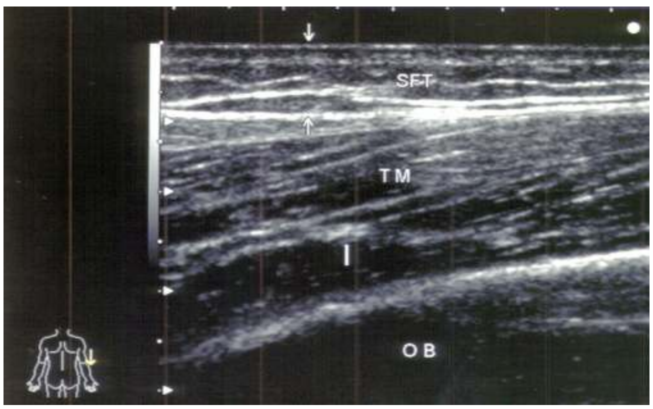
(**A**)



(**B**)



(**C**)

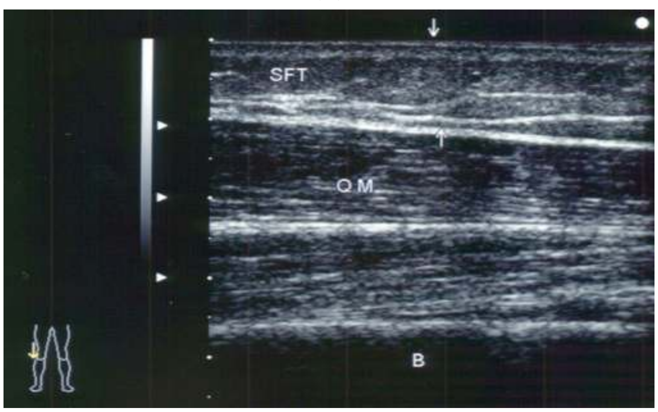
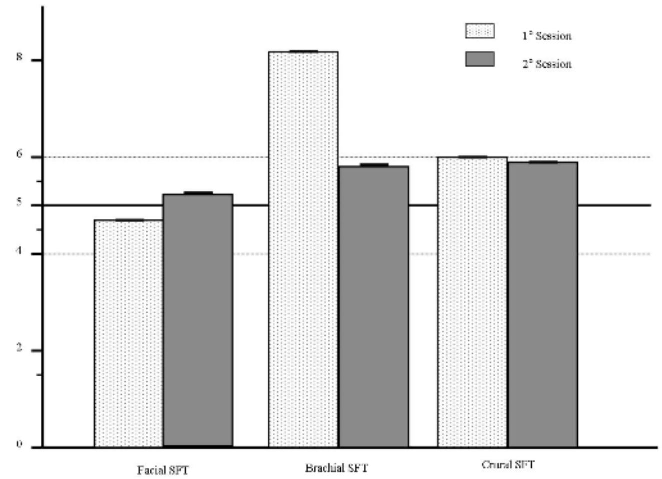


Fig. (1). Sonographic reference points for the assessment of subcutaneous fat thickness related to the body fat changes described in the HARS. US scan with 7.5-13 MHz linear transducers is performed with no pressure on the underlying skin. (**A**) Facial LA: SFT is measured with a left nasogenian transversal scan from the malar bone (MB) to the hyperechoic line corresponding to corneous layer of epidermidis (S) on deepest point of Bichat pad (BP). (**B**) Brachial LA: SFT is measured with a long scans 10 centimetres above the right elbow from superficial fascia of triceps muscle (T M) upper omeral bone (OB) to the hyperechoic line corresponding to corneous layer of epidermidis (S). (**C**) Crural LA: SFT is measured with long scans 15 centimetres above the rotula, from superficial fascia of quadriceps muscle (QM) upper the femoral bone (B) to the hyperechoic line corresponding to corneous layer of epidermidis (S).

(**A**)



(**B**)

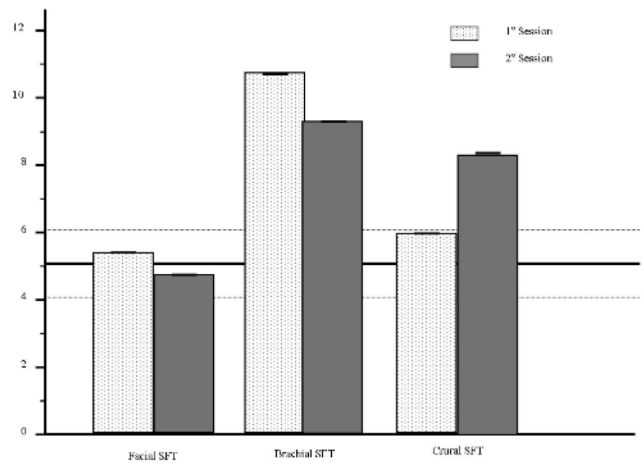


Fig. (2). Intra observer variability of Experienced and Untrained Sonologist in the sonographic measurements of subcutaneous fat thickness.

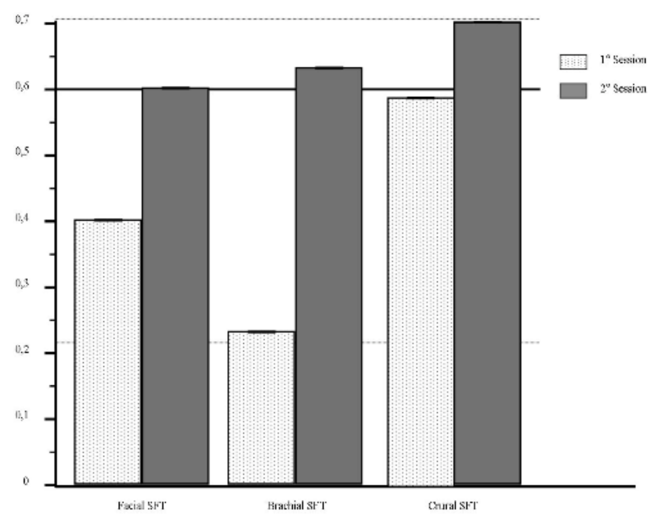


Fig. (3). Inter rate agreement (*kappa*) between the Sonologists in the single sessions. The agreement was quantified by the *kappa (k)* statistic: k is 1 when there is perfect agreement between the classification system; 0 when there is no agreement better than chance; the strength of agreement is poor when $k<0.20$, fair when $k<0.40$, moderate when $k<0.60$, good with $k<0.80$, excellent with $k>0.80$.

this facial SFT measurement's technique and it seem to correctly diagnose high percentages of facial LA compared to the clinical assessments. The high level of agreement with the CT assessments suggests that it is simple and more reliable than more peripheral RPs [6, 8].

4) Therefore, although the authors [1], that assessed the same RP, shows disappointing results, we feel that a not optimized measurement's technique could have influenced their results. This opinion is strengthened by the high intra- and inter-observer variability reported by Padilla *et al*. [1] (~ 31% and 32%, respectively based on 6 assessments by 3 radiologists for only 2 patients) as compared to that observed in other studies (2.6-3.5%) [9]. We investigated intra and inter-observer's variability of facial, brachial and crural SFT assessments made by an experienced and an untrained sonologist. Each sonologist performed 3 consecutive measurements of 20 lipoatrophic patients during two separate sessions, using an EUB 8500 (HITACHI Medical System). Coefficients of variability (SD/mean x100) were similar for the facial (ranges: 4.7-5.2% *vs* 4.9-5.6%, respectively), brachial (range 5.8-8.4% *vs* 9.7-11.2%) and crural SFTs (ranges 5.9-6% *vs* 6.2-8.7%). There was greater consistency in the measurements performed by the experienced *vs* the untrained worker suggesting the need for standardized training to achieve the better reliability (Fig. **2a**,**b**).

Inter-observer agreement as assessed by means of kappa statistic (k) analysis confirmed increased measurement agreement in the assessments of facial (k ranged from 0.40 to 0.60), brachial (k: 0.23-0.63) and crural RP (k: 0.58-0.70) from the 1st to the 2nd session with definitive good agreement (Fig. **3**). We are currently enlarging our experience in a multicentric study with similar encouraging reports on the efficacy of training performed by the same experienced teacher.

In conclusion, if several reports [4-10] show that US can be used to accurately identify HARS-related BFCs, the use of a well-defined and standardized measurement technique is required in order to optimize the reliability and utility of US-mediated BFC assessment, beginning with the careful identification and measurement of RPs, avoiding any bias such as the pressure offered by stand off pads in the skin, and taking care in excluding artefacts due to the too abundant quantity of gel in order to obtain, with minimal transducer pressure, the best resolution of RPs such as indicated in Fig. (**1**).

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