A STRAIGHTFORWARD MULTIPARAMETRIC QUALITY CONTROL PROTOCOL FOR PROTON MAGNETIC RESONANCE SPECTROSCOPY: VALIDATION AND COMPARISON OF VARIOUS 1.5 T AND 3 T CLINICAL SCANNER SYSTEMS

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ABSTRACT

Purpose: The aim of this study was to propose and validate across various clinical scanner systems a straightforward multiparametric quality assurance procedure for proton magnetic resonance spectroscopy (MRS).

Methods: Eighteen clinical 1.5T and 3T scanner systems for MRS, from 16 centres and 3 different manufacturers, were enrolled in the study. A standard spherical water phantom was employed by all centres. The acquisition protocol included 3 sets of single (isotropic) voxel (size 20 mm) PRESS acquisitions with unsuppressed water signal and acquisition voxel position at isocenter as well as off-center, repeated 4/5 times within approximately 2 months. Water peak linewidth (LW) and area under the water peak (AP) were estimated.

Results: LW values [mean(standard deviation)] were 1.4(1.0) Hz and 0.8(0.3) Hz for 3T and 1.5T scanners, respectively. The mean(standard deviation) (across all scanners) coefficient of variation of LW and AP for different spatial positions of acquisition voxel were 43%(20%) and 11%(11%), respectively. The mean(standard deviation) phantom T_2 values were 1145(50) ms and 1010(95) ms for 1.5T and 3T scanners, respectively. The mean(standard deviation) (across all scanners) coefficients of variation for repeated measurements of LW, AP and T_2 were 25%(20%), 10%(14%) and 5%(2%), respectively.

Conclusions: We proposed a straightforward multiparametric and not time consuming quality control protocol for MRS, which can be included in routine and periodic quality assurance procedures. The protocol has been validated and proven to be feasible in a multicentre comparison study of a fairly large number of clinical 1.5T and 3T scanner systems.

1. Introduction

In vivo proton magnetic resonance spectroscopy (MRS) provides unique biochemical information which can complement magnetic resonance imaging (MRI) examinations. Accordingly, MRS is widely employed in several brain as well as body (e.g. breast, prostate, liver) clinical applications [1-4].

Quality Assurance (QA) is recommended in conventional MRI and a number of protocols – such as that proposed by the American Association of Physicists in Medicine (AAPM) [5] or the American College of Radiology (ACR) [6], as well as that based on Eurospin test objects [7] – have been proposed and used. However, these protocols are not sufficient to guarantee the reliability of MRS, as well as of non-conventional techniques of diffusion-weighted imaging (DWI) [8-10] and functional MRI (fMRI) [11-13], and the need of specific QA protocols in advanced and quantitative techniques is still established and recognized [5, 6].

A preliminary European research project aimed to define specific procedures for MRS quality assurance, developing test objects and methodologies [14-17]. These procedures have been validated in a multicenter trial involving 10 sites [17]. Some studies have proposed QA methods for MRS based on home-built dedicated phantoms [18-21], which however hamper the wide use of these methods. The report of the AAPM Task Group #9 [22] dealt with the topic of clinical MRS, giving a number of general recommendations about QA. Also, the AAPM report no. 100 on acceptance testing and quality assurance procedures for MRI facilities [5] has summarized some MRS acceptance tests - which include the assessment of volume of interest (VOI) localization, signal-to-noise ratio (SNR), full width at half maximum (FWHM) of metabolite peaks in the spectrum and amplitude fluctuations - indicating to acquire short echo time sequences with and without eddy currents correction algorithm. Based mainly on theoretical concepts, the AAPM report no. 100 [5] has suggested a VOI localization accuracy within ±1 mm, a global water peak FWHM < 7 Hz and < 14 Hz for an MR scanner system with a second order shim set and with only linear shim, respectively. Also, the AAPM report no. 100 [5] has proposed a test for scanner hardware

stability, which consists in visually inspect the remnant water peak signal from subsequent water-suppressed water signal acquisitions – the recommended amplitude fluctuations are less than 10%. One can analyze also the unsuppressed water signal by turning off the water suppression radiofrequency pulses. In this case, shot-to-shot signal amplitude variation should be approximately less than 1% and the peak position should not change by more than 1 Hz. Nonetheless, so far only few recommendations have been given and some of them can not be performed easily by users of scanner systems for clinical MRS. Furthermore, a consensus about acceptable tolerance values of measured quality control indices is lacking. For these reasons we believe that a specific QA protocol for MRS, which can be applied routinely to most clinical scanners, can be of practical interest. In this regard, multicenter comparison studies can be useful to validate QA protocols as well as to obtain a range of variation across scanners of quality indices, which can represent an indicative and empirical reference for a centre that goes ahead to apply a quality assurance protocol for MRS.

Toward a standardized QA in routine as well as in research studies, a widely accepted and easily applicable quality control protocol for MRS – which can be used for scanner systems with different characteristics/performances – is advisable. The aim of this preliminary study was hence to propose a straightforward MRS quality assurance procedure and validate it on a fairly large number of different scanner systems by 3 different manufacturers. In particular, 16 centres (18 scanner systems) were enrolled in the study among the attendees of the workgroup "Quantification and Intercomparison in MRI" of the Italian Association of Medical Physics (AIFM).

2. **Materials and methods**

2.1. Scanner systems and phantom

Eighteen clinical 1.5 T (12) and 3 T (6) scanner systems for MRS, from 16 centres and different manufacturers, were enrolled in the study (Table 1). For each scanner system, standard maintenance and quality assurance procedures were routinely performed.

A standard spherical (diameter 15 cm) doped water phantom (1 mM $NiCl_2$ and 0.5 g/l NaN_3) was employed by all centres enrolled in the study.

2.2. Acquisition protocol

All acquisitions were performed by using the head coil (Table 1) at fixed signal gain. The phantom was placed in the magnet room at least 6 hours before acquisitions to reach thermal equilibrium. Moreover, the phantom was positioned in the centre of the head coil at least 5 minutes before starting the acquisitions.

The acquisition protocol included 3 sets of single voxel PRESS sequences (a-c) without water signal suppression. In particular, for each acquisition sequence, all the participating centres performed the following procedures:

a) To place the acquisition voxel in the centre of the phantom; to set voxel size (isotropic) of 10/15/20/25/30 mm, echo time (TE) of 30 ms, repetition time (TR) of 4000 ms, number of averages of 16, phase cycle of 16, samples number of 1024, bandwidth of 1000 Hz and 2000 Hz for 1.5 T and 3 T scanners, respectively;

b) To place in the centre of the phantom as well as 4 cm off-centre along superior/inferior and left/right directions an isotropic voxel with size of 20 mm; to set TE of 30 ms, TR of 4000 ms, number of averages of 16, phase cycle of 16, bandwidth of 1000 Hz and 2000 Hz for 1.5 T and 3 T scanners, respectively;

c) To place the acquisition voxel in the centre of the phantom; to set an isotropic voxel with size of 20 mm, TE of 30/100/150/300/400 ms, TR of 4000 ms, number of averages of 16, phase cycle of 16, samples number of 1024, bandwidth of 1000 Hz and 2000 Hz for 1.5 T and 3 T scanners, respectively.

In order to obtain an almost complete recovery of longitudinal magnetization, a relatively long TR was employed. According to Drost et al [22], a relatively short TE was used (except for T_2

estimation, which needed acquisitions with multiple TEs). The total acquisition time of the entire protocol was approximately 12 min.

The protocol was acquired a number of times within 2 months. In particular, acquisitions were repeated 5 and 4 times for 15 and 3 scanner systems, respectively.

2.3. Data processing and analysis

Each centre processed acquired data by means of jMRUI software [23-25]. In order to fit the water peak in the time domain, the Hankel-Lanzos square singular value decomposition (HLSVD) method [26] was employed, with a number of components of 1. Linewidth (i.e. FWHM of the peak) (LW) and amplitude (i.e. area under the peak) (AP) values of water peak were finally obtained and recorded. All the processed data were sent to the coordinating centre of the intercomparison for further analyses.

Based on data obtained from acquisition described in a) (see above), any linear dependence of AP on acquisition voxel volume was assessed by estimating the linear correlation coefficient (r). In order to allow comparison of scanner systems independently of the specific signal gain, AP and acquisition voxel volume were normalized to the corresponding values of acquisition voxel with 20 mm size (isotropic), obtaining a theoretically expected linear regression line ($y = mx + q$) of AP as a function of acquisition voxel volume [22], with slope (m) of 1.

By using data with isotropic voxel size of 20 mm, the coefficient of variation (defined as the standard deviation divided by the mean value) of LW and AP for repeated measurements (CV_{time}) was calculated. Similarly, by using data from acquisitions described in b) (see above), the CV of LW and AP measurements for different acquisition voxel positions ($CV_{position}$) was computed for each measurement session.

In order to estimate phantom T_2 relaxation time, the following equation was fitted to data from acquisitions described in c) (see above):

$$AP(TE) = AP_0 \exp(-TE/T_2) \quad (1)$$

where AP_0 is the AP value at TE = 0. Also, the CV_{time} of T_2 was calculated.

3. Results

LW results, in terms of mean value in the central voxel and coefficient of variation for different acquisition voxel positions are reported in Figure 1 and in Figure 2, respectively. Coefficients of variation of LW for repeated measurements are reported in Table 2. In particular, 10 scanners (56%) showed LW values lower than 1 Hz, 7 scanners (39%) showed LW values within 1 Hz and 2 Hz, and only one 3 T scanner showed LW value greater than 3 Hz (Fig. 1). The average of LW across scanners was 1.4 Hz and 0.8 Hz at 3 T and 1.5 T, respectively, corresponding to approximately 0.012 ppm in both cases. Eight scanners (44%) were characterized by $CV_{position}$(LW) values ranging from 16% to 32%, the other 10 scanners (56%) were characterized by $CV_{position}$(LW) values between 40% and 77%. Thirteen scanners (72%) showed CV_{time}(LW) values ranging from 8% to 20%, and only 2 scanners showed CV_{time}(LW) values greater than 50%.

AP results in terms of coefficient of variation for different acquisition voxel positions and coefficient of variation for repeated measurements are reported in Figure 3 and in Table 2, respectively. For 16 scanners (89%), $CV_{position}$(AP) values ranged from 1% to 14%, and only 2 scanners were characterized by $CV_{position}$(AP) values greater than 25%. Fifteen scanners (83%) showed CV_{time}(AP) values ranging from 1.8% to 11%, and only 3 scanners showed CV_{time}(AP) values greater than 25%.

For each scanner system, the normalized AP showed a significant ($p < 0.01$) linear dependence on the normalized voxel volume ($r > 0.99$ and 0.95 for 1.5 T and 3 T scanner systems, respectively), with slope of the regression line ranging from 0.91 to 1.12 (Fig. 4).

Mean T_2 value was 1145 ms and 1010 ms for 1.5 T and 3 T scanners, respectively (Fig. 5). In particular, $CV_{time}(T_2)$ values were below 10% for all scanners, and there was no appreciable difference between 1.5 T and 3 T scanners (Table 2).

4. Discussion

Given that MRS is widely employed in clinical routine, a specific quality control program is recommended for this non conventional MRI technique. In this multicenter study, a straightforward and not time consuming MRS quality control protocol has been proposed and validated. This protocol, which is based on a standard water phantom and single voxel acquisitions, can be easily implemented on most clinical scanners to check MRS acquisitions in particular, as well as some basic performance of scanners in general. To the best of our knowledge, no study on MRS quality controls has enrolled 18 scanners or more. A previous study [17], with main purpose to assess acquisition voxel localization, has included only 10 scanners.

While a number of previous study aimed to propose specific quality controls for MRS, they require ad hoc phantoms and time consuming procedures that can be hence unlikely suitable for routine quality controls. For instance, Song et al [22] have introduced a phantom for QA in conventional MRI and MRS, which was characterized by several containers filled with different solutions of metabolites; the whole acquisition procedure needed 75-90 minutes to be carried out. Rice et al [19] and Woo et al [20] have described an antropomorphic MRS head phantom and cone-shape phantom for multi-voxel MRS, respectively. Also, while Drost et al [22] and Jackson et al [5] have discussed the fundamental requirements of an effective protocol for QA in MRS, they did not aim to examine in detail procedures and quality indices. On the other hand, the MRS quality control protocol proposed in this study is multiparametric and requires only 10-15 minutes for the acquisition of a typical water phantom (as that suitable to conventional MRI quality controls). In particular, all centres enrolled in the study employed a standard water phantom, in order to allow comparison of different scanner systems.

Local magnetic field uniformity (which affects LW values and depends on various factors including shimming) of high degree is fundamental to carry out reliable qualitative as well as quantitative MRS studies. In this regard, except for only one 3 T scanner, we found LW values lower than 2 Hz (i.e. < 0.015 ppm) for 3 T scanners and lower than 1.3 Hz (i.e < 0.020 ppm) for 1.5

T scanners (Fig. 1). Nonetheless, $CV_{position}$(LW) results (Fig. 2) indicate that local magnetic field uniformity can vary appreciably with acquisition voxel position.

In MRS, the assessment of acquisition voxel selection is challenging. The approach proposed in previous studies [17, 18] requires the use of specific phantoms with different compartments. Jackson et al [5] have used a method based on imaging techniques to check whether the effectively selected acquisition voxel corresponds to the nominal one. However, these methods could result not easy for routine quality controls of clinical scanners. In this study, we aimed to assess only acquisition voxel volume, founding a linear dependence of AP on acquisition voxel volume for all scanner systems. Moreover, all scanners showed only a limited difference (±12%) between the measured and expected value (i.e. 1) of slope of the regression line of normalized AP as a function of normalized acquisition voxel volume (Fig. 4), which could indicate a signal offset or a slight mismatch between the effective and nominal acquisition voxel volume. In this regard, we note that the variation of AP with spatial position of acquisition voxel is relatively small for most scanners [i.e. $CV_{position}(AP) < 15\%$].

In a recent quality assurance comparison of different scanners for quantitative DWI [8], the apparent diffusion coefficient (ADC) was used to assess scanner performances, with particular reference to gradients. Similarly, T_2 represents a physical property of the phantom solution which can be used to assess basic performances of different scanner systems for MRS. Indeed, in this QA protocol for MRS, T_2 estimation depends on AP (i.e. acquisition voxel volume) and TEs (i.e gradients and radiofrequency system performances) (see Eq. 1). The results were considered separately for 1.5 T and 3 T scanners, given that T_2 is expected to decrease slightly with increasing magnetic field strength [27]. Accordingly, the mean phantom T_2 was slightly higher for 1.5 T scanners (1145 ms) than 3 T scanners (1010 ms). Among the analyzed quality indices, T_2 (as well as AP) showed the lowest variations for repeated measurements over time.

In general, the scanners enrolled in this study showed fairly similar performances. However, a 3 T scanner (i.e. 1a) was characterized by relatively anomalous values of LW and $CV_{position}$(AP)

(Figs. 1 and 3), and another 3 T scanner (i.e. 4a) showed relatively low T_2 estimates (Fig. 5). Also, a 1.5 T scanner (i.e. 12b) was characterized by relatively high values of CV_{time}(LW) and CV_{time}(AP) (Table 2). Notably, given that standard and routine quality assurance programs indicated no substantial alteration of functional performances for all scanner systems, additional specific QA procedures for MRS could have hence the potential to reveal/monitor subtle and early changes in functioning of a scanner system.

Jackson et al [5] have proposed the use of a water phantom containing various metabolites, allowing to measure metabolite-to-water peak area ratio, which could represent an additional check in quality assurance of scanner systems for quantitative MRS. However, such an approach lengthens acquisition time, depends on type/concentration of employed metabolites and requires chemically stable solution over time, hampering the wide use of this method for routine quality controls of clinical scanners. Previous studies [19, 20, 22] have designed QA procedures focused on metabolites quantification. However, given the low SNR of metabolites MRS acquisitions, these procedures require fairly long acquisition time and are prone to possible uncertainties in metabolites quantification. On the other hand, unsuppressed water signal acquisitions are still appropriate to check basic scanner performance in MRS (e.g. local magnetic field uniformity, acquisition voxel volume).

The validation of a quality control protocol in a multicentre comparison study of several scanners can provide reference values of measured quality indices. Indicative reference values of LW, as well as of $CV_{position}$(LW) and $CV_{position}$(AP), can be obtained as the mean ± 2 standard deviation values across 1.5 T and 3 T scanners separately. Moreover, in periodic quality controls, it can be assumed that a normal variation over time of LW, AP and T_2 is associated with a coefficient of variation less than the mean + 2 standard deviation across scanners of CV_{time}(LW), CV_{time}(AP) and CV_{time}(T_2), respectively. Nonetheless, each centre implementing routinely the quality control protocol can detect long-term stability of measures by adopting, for instance, rules based on Shewhart charting [28-30].

In order to better assess reference values of quality control indices in MRS, we plan to extend our comparison study to a greater number of participating centres. Also, our quality control protocol for MRS could be improved by adding chemical shift imaging (CSI) acquisitions, in order to include assessment of multivoxel MRS.

5. Conclusions

We proposed a straightforward multiparametric and not time consuming quality control protocol for MRS, which can be included in routine and periodic quality assurance procedures. The protocol has been validated and proven to be feasible in a multicentre comparison study of a fairly large number of 1.5 T and 3 T scanner systems by different manufactures.

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Figure legends:

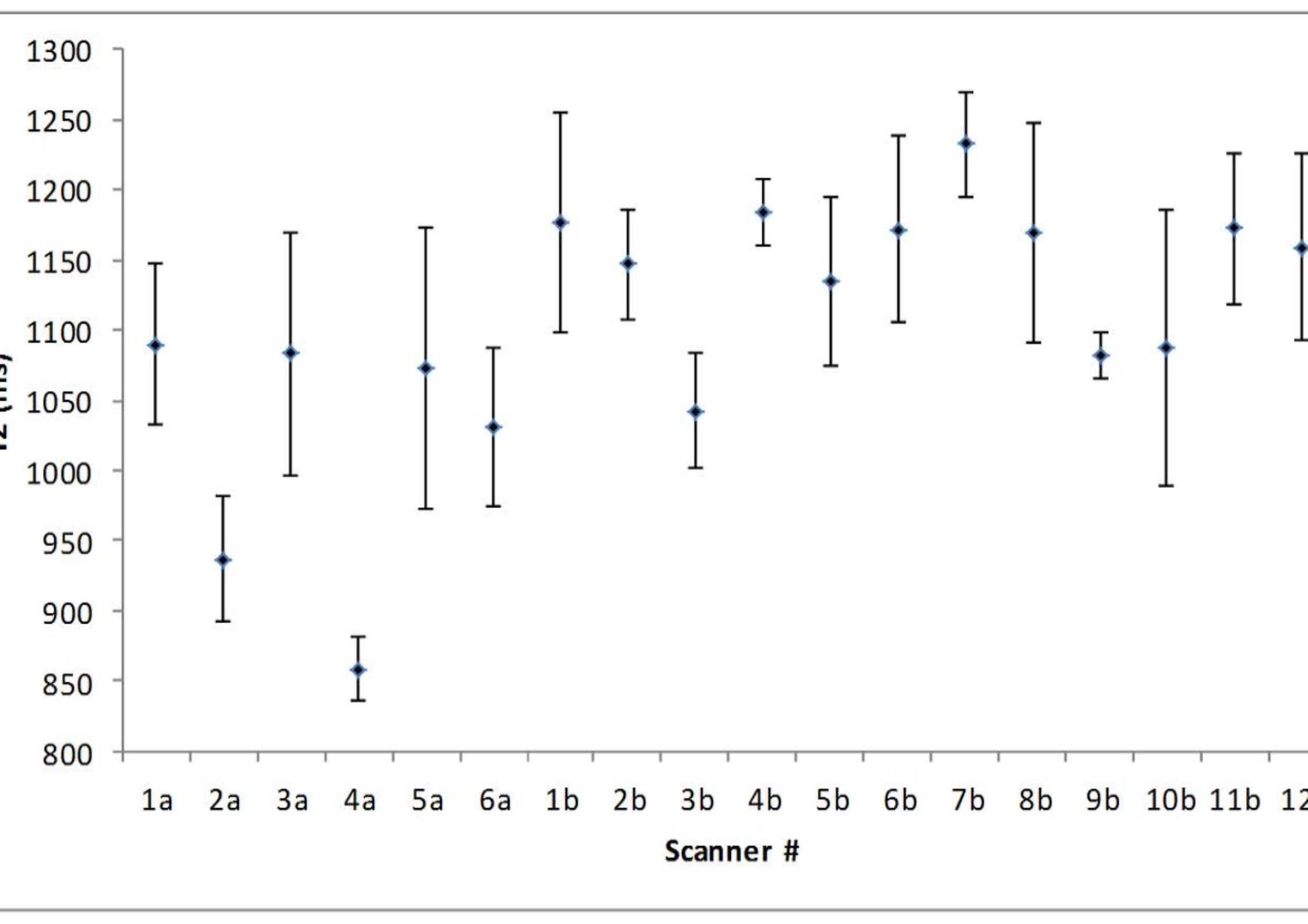
Figure 1. Linewidth (LW) of water peak for each scanner. The dots and error bars represent the mean value and standard deviation across repeated measurements, respectively. The suffix "a" and "b" indicate 3 T and 1.5 T scanners, respectively. (Isotropic voxel with size of 20 mm, placed in the centre of phantom).

Figure 2. For each scanner, coefficient of variation of LW for different acquisition voxel positions, $CV_{position}$(LW). The dots and error bars represent the mean value and standard deviation across repeated measurements, respectively. The suffix "a" and "b" indicate 3 T and 1.5 T scanners, respectively. (Isotropic voxel with size of 20 mm).

Figure 3. For each scanner, coefficient of variation of AP for different acquisition voxel positions (i.e. centre and 4 cm off-centre along orthogonal directions), $CV_{position}$(AP). The dots and error bars represent the mean value and standard deviation across repeated measurements, respectively. The suffix "a" and "b" indicate 3 T and 1.5 T scanners, respectively.

Figure 4. For each scanner, slope (m) of the regression line ($y = mx + q$) of normalized AP as a function of normalized acquisition voxel volume. The dots and error bars represent the mean value and standard deviation across repeated measurements, respectively. The suffix "a" and "b" indicate 3 T and 1.5 T scanners, respectively.

Figure 5. Relaxation time T_2 for each scanner. The dots and error bars represent the mean value and standard deviation across repeated measurements, respectively. The suffix "a" and "b" indicate 3 T and 1.5 T scanners, respectively.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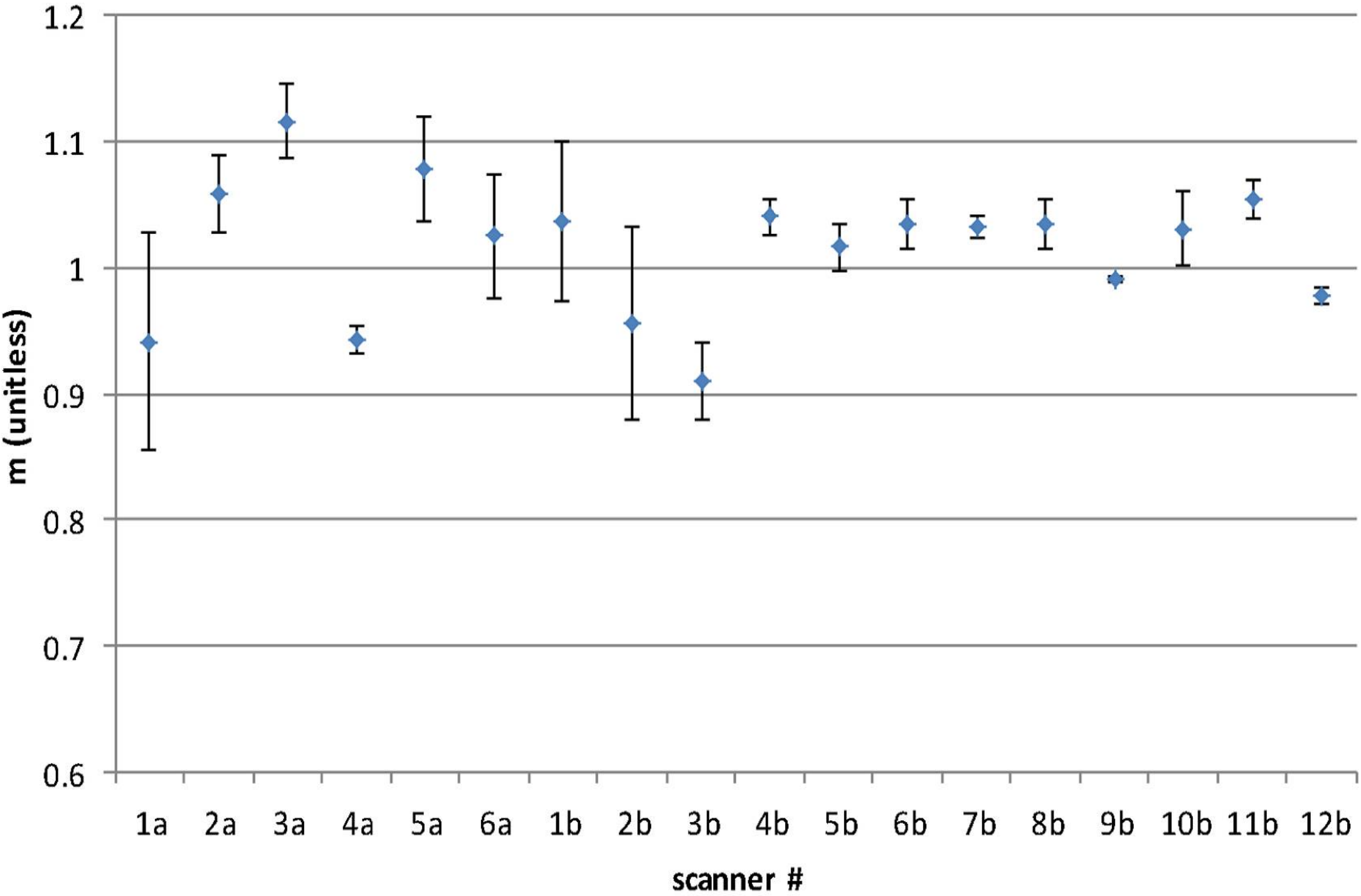
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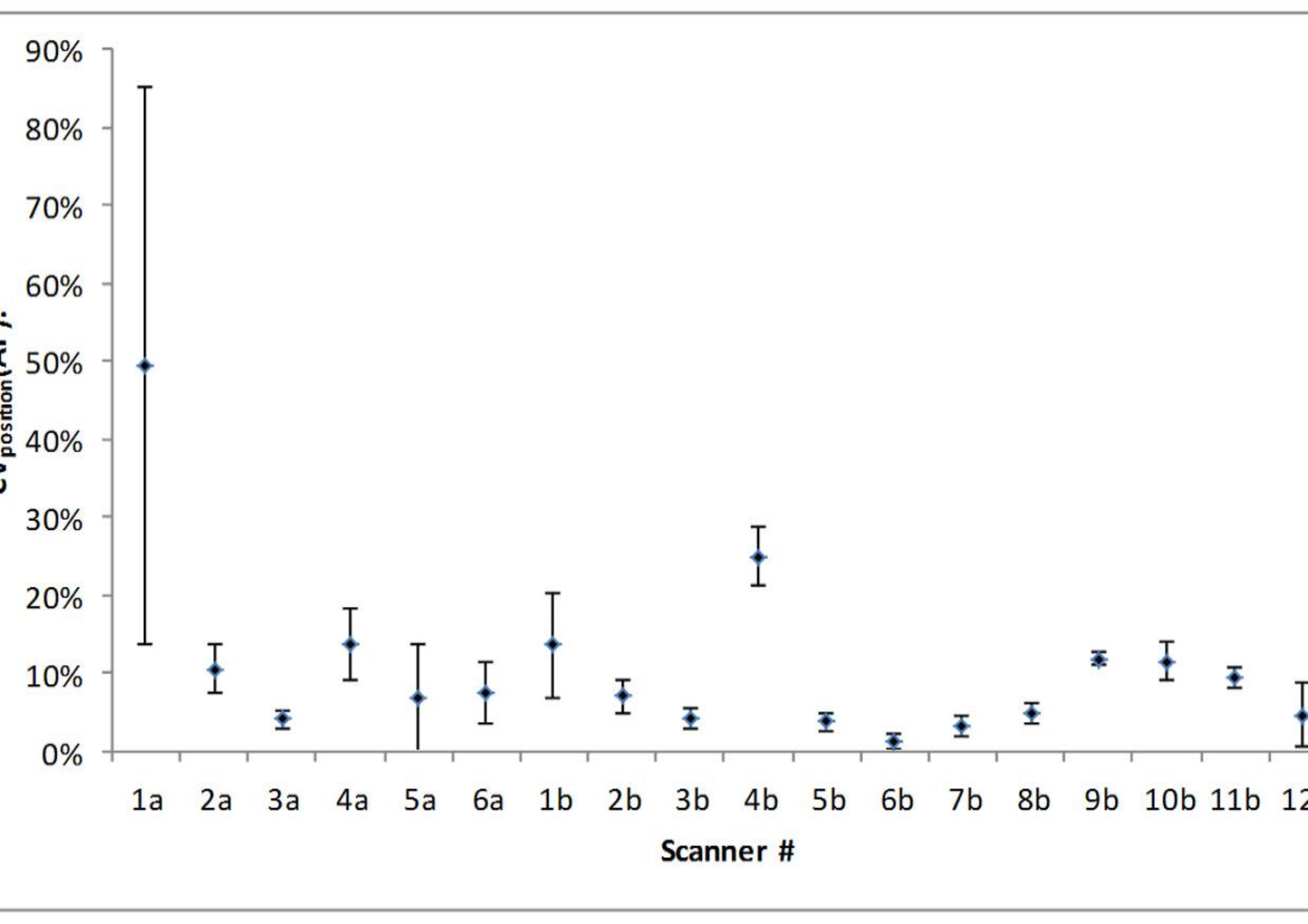
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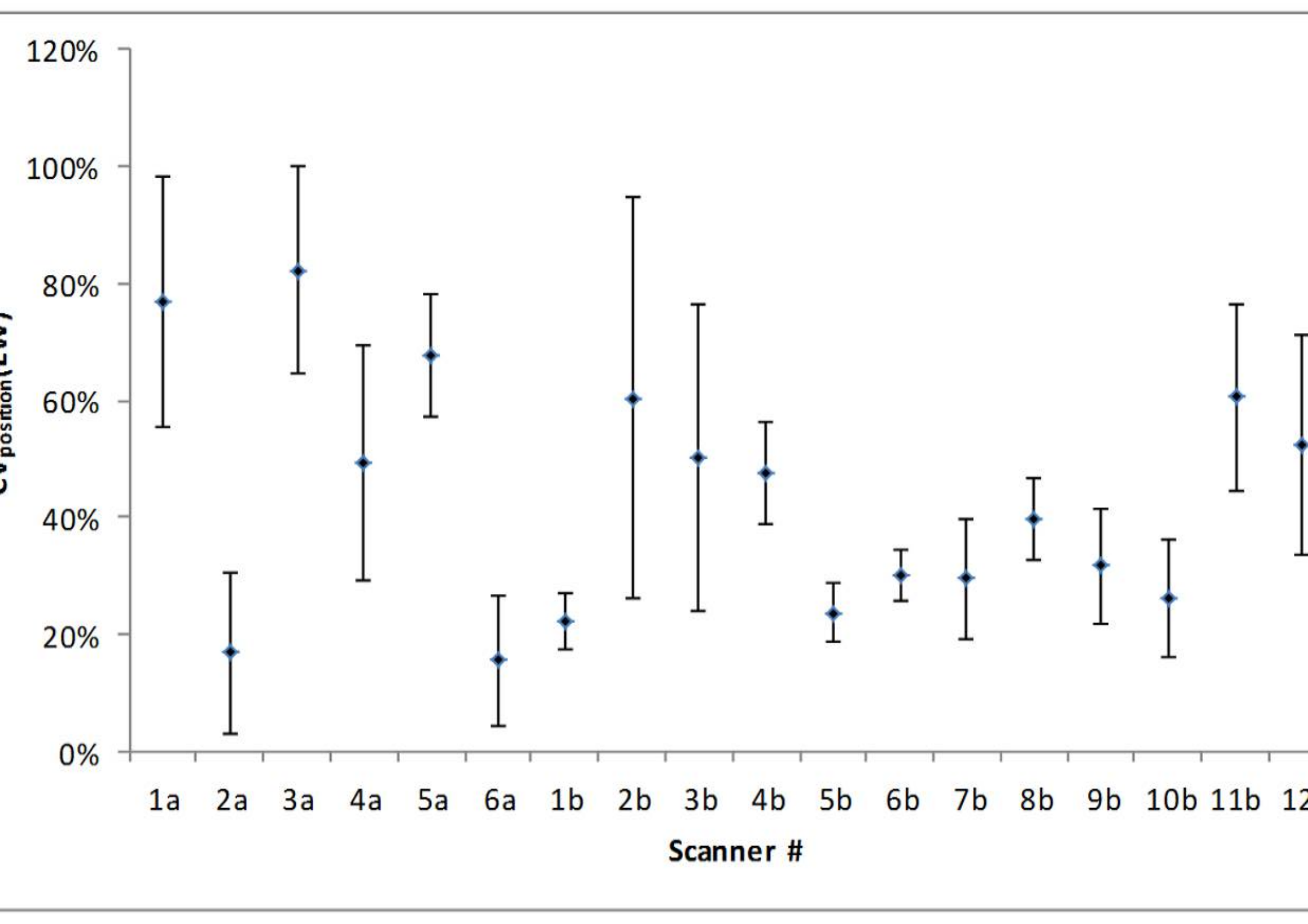
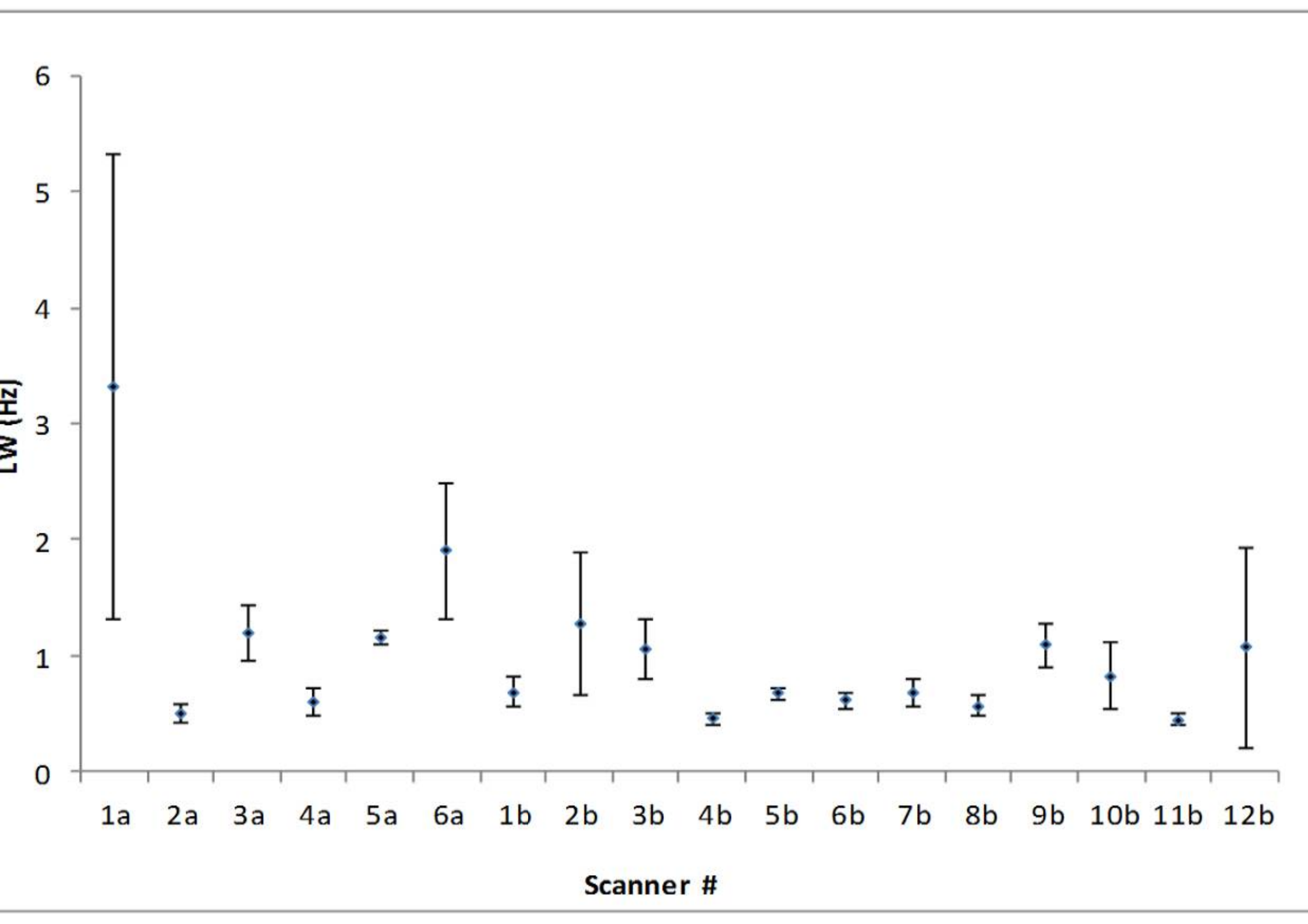
9b
10b
11b
12
Scanner #


120%
100%
80%
60%
40%
20%
0%
1a
2a
3a
4a
5a
6a
1b
2b
3b
4b
5b
6b
7b
8b
9b
10b
11b
Scanner #


6
5
4
3
2
1
0
LW (Hz)
1a
2a
3a
4a
5a
6a
1b
2b
3b
4b
5b
6b
7b
8b
9b
10b
11b
12b
Scanner #