Estimation of acute fluid shifts using bioelectrical impedance analysis in horses.

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Running Title: MF-BIA in horses

A portion of this study will be presented at the 2006 ACVIM Forum as an abstract.

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Abstract:

Background: Multi-frequency bioelectrical impedance analysis (MF-BIA) has been used to evaluate extracellular fluid volume (ECFV), but not fluid fluxes, in horses. If able to detect acute changes in ECFV, MF-BIA would be useful in monitoring fluid therapy in the ICU.

Hypothesis: The purpose of this study was to evaluate the ability of MF-BIA to detect acute fluid changes in horses. We hypothesized that MF-BIA would detect clinically relevant (10-20%) changes in ECFV.

Animals: Six healthy mares.

Methods: Original experimental study. Mares were studied in three experiments: 1) crystalloid expansion of euhydrated subjects, 2) furosemide-induced dehydration followed by crystalloid administration, 3) acute blood loss followed by re-administration. MF-BIA measurements were made before, during, and after each fluid shift and compared to known changes in volume calculated based on the intravenous fluids that were administered in addition to urinary losses. Mean errors between MF-BIA estimated change and known volume change were compared using nonparametric ANOVA. Estimated ECFV pre- and post-fluid administration were similarly compared. Level of statistical significance was set at p<0.05.
Results: Results of the study showed a statistically significant change in ECFV and TBW during crystalloid expansion and dehydration. Statistically significant changes were not observed during blood loss and administration. Mean errors between MF-BIA results and measured net changes were small.

Conclusions and clinical importance: MF-BIA represents a practical and accurate means of assessing acute fluid changes during dehydration and expansion of ECFV using isotonic crystalloids with potential clinical applications in equine critical care.
Acute shifts in body fluids occur frequently in critically ill patients, but accurate quantification of these changes continues to be a challenge. Weight change, biochemical indices, and dilutional techniques have been utilized to estimate fluid losses or gains, but these have limitations. Specifically, weight changes cannot distinguish between losses from the extracellular fluid volume (ECFV) and intracellular fluid volume (ICFV). Knowing the balance between these specific fluid spaces is essential to guiding therapy in the clinical setting. Use of biochemical indices, such as changes in packed cell volume (PCV) and total plasma protein concentration, requires knowledge of baseline values and may not be reliable under conditions of acute blood loss, anemia, splenic contraction, hypoproteinemia and hyperproteinemia. Markers of acid-base balance such as blood lactate concentration, base excess, and pH can be suggestive of deficits within the vascular space, but they are not specific to hypovolemia nor do they provide quantitative estimates of fluid losses. Dilutional techniques, such as bromide and deuterium administration, are considered the gold standard for the determination of ECFV and total body water (TBW) volume, respectively. However, they are not clinically applicable in situations of rapidly changing fluid balance as they require time to reach steady state and prolonged equilibration periods, and as such they are not practical for every day clinical use.

Multi-frequency bioimpedance analysis (MF-BIA) is a technology that has been used to assess fluid volume in humans and a number of animal species, including horses. It utilizes an alternating low-frequency electrical current to make predictions about body composition based on the assumption that fat and bone are poor conductors of electricity, as opposed to biological fluids which conduct currents well.
MF-BIA is capable of providing rapid, non-invasive estimates of ECFV, ICFV, and total body water (TBW) by determining the resistance and reactance properties of tissues. This latter information is then applied to a model requiring the length between conductors and the body weight, in order to calculate fluid volume compartments.

Bioimpedance analysis has been used to detect acute changes in fluid volumes in humans. Fluid loss due to exercise, diuretic administration, and hemodialysis have been evaluated. Fluid gain, as a result of intravenous crystalloid and oral fluid administration, has been examined as well. Most of the studies indicate that MF-BIA is more reliable during altered fluid states in which electrolyte concentrations remain stable (isotonic dehydration or rehydration). Up to this time, there have been no studies evaluating BIA as a measure of fluid changes in acute blood loss or blood product administration in any species. Additionally, most studies employing BIA have focused on the evaluation of a single fluid imbalance, while there are only a few studies comparing multiple fluid shifts in the same patient. There are no published studies evaluating BIA for assessing acute fluid shifts in horses other than those occurring during exercise.

The purpose of this study was to evaluate the ability of MF-BIA to detect acute fluid changes in an animal model: crystalloid expansion in euhydrated subjects, furosemide-induced dehydration, crystalloid administration to dehydrated subjects, acute blood loss, and administration of whole blood. First, we tested the hypothesis that MF-BIA would detect a statistically significant change in ECFV for each of these fluid shifts. Second, we described the observed change in the fluid compartments as compared to a known change in body water due to urine loss or fluid administration. Third, we
compared the accuracy of MF-BIA to detect volume fluxes during experimental
alterations in fluid volume as compared to actual measured changes.
MATERIALS AND METHODS

Six clinically healthy mares were studied and included Thoroughbreds, Quarter Horses, Arabians, as well as horses of mixed breeding. The study was approved by the University Animal Use and Care Administrative Advisory Committee of the University of California, Davis. All horses were held off feed for 12 hours prior to the start of the study and no water or feed was provided during the measurement period.

Horses were restrained in standing stocks during the measurements for each experiment of the trial. All metal surfaces were covered with plastic coverings. Body weight was measured in all horses immediately prior to the start of the procedure using a digital walk-on scale and horses ranged in weight from 453.4 to 578.9kg. The distance from the ground to the top of the shoulders (withers) was determined using a measuring tape as previously described.2

A 10-ga jugular catheter was placed and used for blood sample collection and fluid administration. Additionally, a 30-French Foley urinary catheter was placed in the bladder of all mares and attached to a urinary collection system. Bioimpedance measurements were made using the previously described ‘head-tail configuration’ due to ease and tolerance of electrode placement.2 Briefly, the hair was shaved in a 4cm X 4cm patch over the right cranial border of the first cervical vertebrae and over the caudal aspect of the region of the right tuber ischii. The skin surfaces were cleaned with alcohol and allowed to dry. Subdermal platinum electrodes were then placed 2.5cm apart in a configuration parallel to the ground surface within the shaved areas. An adhesive glue was used to hold the electrodes in place throughout the study.
A bioimpedance analyzer was attached to the subdermal electrodes and used to predict the ECFV, ICFV, and TBW according to a previously described model for horses. Briefly, both resistance and reactance were obtained at 50 frequencies ranging from 5 to 1000 kHz. The impedance and phase angle were then computed from these measured values and used to determine the resistance of extracellular and intracellular water. The equations used to estimate extracellular, intracellular, and total body fluid volumes in horses have been previously described.

In addition to the bioimpedance measurements described below, the following measurements and calculated values were recorded for comparison. ‘Baseline’ is defined as the measurements made at the start of each experiment, before any fluid shifts (dehydration or intravenous fluid administration) occurred.

\[
\Delta V(t) = V_I(t) - U_O(t) \quad \text{(Equation 1)}
\]

Where \(\Delta V(t)\) is the measured (net) change in volume from baseline, \(V_I(t)\) is the total intravenous volume infused since baseline and \(U_O(t)\) is the total urinary output since baseline.

\[
\Delta \text{ECFV}_{MF-BIA(t)} = \text{ECFV}_{MF-BIA(t=0)} - \text{ECFV}_{MF-BIA(t)} \quad \text{(Equation 2)}
\]

Where \(\Delta \text{ECFV}_{MF-BIA(t)}\) is the change in ECFV at time ‘t’ as compared to baseline (t=0) for any given time point using MF-BIA determined values.
\[ MF-BIA \text{ ERROR}_{ECFV(t)} = \Delta V(t) - \Delta ECFV_{MF-BIA(t)} \]  
(Equation 3)

Where \( MF-BIA \text{ ERROR}_{ECFV(t)} \) is the error in the change in ECFV predicted by MF-BIA as it compares to the net measured change in volume.

\[ MF-BIA \text{ ERROR}_{ECFV*_{(t)corr}} = \frac{MF-BIA \text{ ERROR}_{ECFV(t)}}{\Delta V(t)} \]  
(Equation 4)

Where \( MF-BIA \text{ ERROR}_{ECFV*_{(t)corr}} \) is the volume-corrected error in the ECFV predicted by MF-BIA as it compares to the net measured change in volume.

\[ \Delta TBW_{MF-BIA(t)} = TBW_{MF-BIA(t=0)} - TBW_{MF-BIA(t)} \]  
(Equation 5)

Where \( \Delta TBW_{MF-BIA(t)} \) is the change in TBW at time ‘t’ as compared to baseline for any given time point using MF-BIA predicted values.

\[ MF-BIA \text{ ERROR}_{TBW(t)} = \Delta V(t) - \Delta TBW_{MF-BIA(t)} \]  
(Equation 6)
Where $\text{MF-BIA ERROR}_{\text{TBW}(t)}$ is the error in the change in TBW predicted by MF-BIA as it compares to the net measured change in volume.

$$\text{MF-BIA ERROR}_{\text{TBW}(t)\text{corr}} = \frac{\text{MF-BIA ERROR}_{\text{TBW}(t)}}{\Delta V(t)} \quad \text{(Equation 7)}$$

Where $\text{MF-BIA ERROR}_{\text{TBW}(t)\text{corr}}$ is the volume-corrected error in the TBW predicted by MF-BIA as it compares to the net measured change in volume.

$$\Delta \text{ICFV}_{\text{MF-BIA}(t)} = \text{ICFV}_{\text{MF-BIA}(t=0)} - \text{ICFV}_{\text{MF-BIA}(t)} \quad \text{(Equation 8)}$$

Where $\Delta \text{ICFV}_{\text{MF-BIA}(t)}$ is the change in ICFV at time ‘t’ as compared to baseline for any given time point using MF-BIA predicted values.

Experiment 1: Normovolemic crystalloid expansion

Baseline bioimpedance measurements were made every five minutes for a total of 20 minutes for a total of 5 measurements, in order to calculate the coefficient of variation. An isotonic crystalloid was then administered at 80ml/kg/hr for 30 minutes for a total dose of 40ml/kg using a peristaltic fluid roller pump. Bioimpedance measurements made
prior to infusion, immediately after infusion, one hour after infusion, and two hours after
infusion were used for comparisons.

Experiment 2: Dehydration and re-hydration with an isotonic crystalloid

After placement of the catheters described above, three baseline bioimpedance
measurements were obtained in succession. A dose of 1mg/kg of furosemide was
administered intravenously and three successive bioimpedance measurements were made
at one-hour intervals over the next four hours during dehydration. At the end of this four
hour period, an isotonic crystalloid was administered at a rate of 20ml/kg/hr over two
hours for a total dose of 40 ml/kg. Bioimpedance measurements made prior to
dehydration, at one-hour intervals during dehydration, at one-hour intervals during
rehydration, and one hour following rehydration were compared.

Experiment 3: Blood loss and administration

After placement of the catheters described above, baseline bioimpedance
measurements were obtained every five minutes for a total of 20 minutes. At this point,
blood collection was performed using a suction pump and collection bags containing
ACD solution in a ratio of 1:10 (ACD solution:blood). The rate of blood collection was
approximately 16 ml/kg/hr over one hour, for a total dose of 16 ml/kg. Thirty minutes
after the end of blood collection, the blood was re-administered at the same rate over one
hour. Bioimpedance measurements made prior to blood loss, immediately following
blood loss, and immediately following blood administration were used for comparisons.
Statistical analysis: All values are reported as median (range). A non-parametric ANOVA (Friedman) with a post-hoc Dunn test was used to compare $ECFV_{MF-BIA(t)}$, $ICFV_{MF-BIA(t)}$, $TBW_{MF-BIA(t)}$ at each time point. The same test was also used to compare $\Delta ECFV_{MF-BIA(t)}$, $\Delta ICFV_{MF-BIA(t)}$, and $\Delta TBW_{MF-BIA(t)}$ at each time point for each phase of the study.

Additionally, the 95% limits of agreement were calculated for each fluid shift (infusion, dehydration, and rehydration) using $MF-BIA \text{ ERROR}_{ECFV(t)}$ according to previously described techniques. The same calculations were made for the $MF-BIA \text{ ERROR}_{TBW(t)}$. The $MF-BIA \text{ ERROR}_{ECFV^{*}(t)}$ was then compared between each phase of the trial using a non-parametric ANOVA (Friedman). Finally, Bland-Altman plots were constructed to evaluate $\Delta V(t)$ with $MF-BIA \text{ ERROR}_{ECFV^{*}(t)}$. In all cases, a $p$-value of < 0.05 was used as a measure of statistical significance.
Results

Coefficient of variation for the MF-BIA technique was calculated from the 5 measurements made at baseline from each of the horses. The mean coefficient of variation for the BIA measurements for ECFV, TBW, and ICFV were 1.1 %, 1.2 % and 1.5 %, respectively.

Results of isotonic crystalloid expansion to normovolemic patients (Experiment 1) are shown in Table 1, Table 2, and Figure 1. There was a statistically significant expansion of the ECFV at end infusion and 1-h, but not at 2-, 3-, or 4-h, post-infusion. There was a statistically significant increase in TBW at the end of the infusion. There was no statistically significant change in the ICFV at any point in time.

Results of the furosemide-induced dehydration (Experiment 2-dehydration phase: Table 3, Table 4, and Figure 2) indicated a statistically significant decrease in the ECFV at 1-h and 4-h following diuretic administration. There was also a statistically significant decrease in TBW at 3-h post. There was no statistically significant change in ICFV at any time point.

Results of isotonic crystalloid rehydration (Experiment 2-rehydration phase: Table 5, Table 6, and Figure 3) showed a statistically significant increase in the ECFV at 2- and 3-h post-rehydration. There was also a statistically significant increase in TBW at 2-h after rehydration. There was a statistically significant decrease in the ICFV at 2-h post rehydration.

Results of the blood loss and blood administration phase (Experiment 3) identified a slight contraction and expansion of the ECF compartment, respectively, though these changes were not statistically significant (Tables 7 and 8).
Figure 4 and Figure 5 show a comparison between the net measured change \( \Delta V(t) \) as compared to the MF-BIA determined changes in total body water and ECFV \( \Delta \text{TBW}_{\text{MF-BIA}}(t) \) and \( \Delta \text{ECFV}_{\text{MF-BIA}}(t) \) at all time points and in all phases combined. The \( \Delta \text{ECFV}_{\text{MF-BIA}}(t) \) was statistically better than the \( \Delta \text{TBW}_{\text{MF-BIA}}(t) \) for determining \( \Delta V(t) \) when using all time points from phase 1 and phase 2 combined \((p<0.0001)\). MF-BIA was statistically better at predicting \( \Delta V(t) \) during dehydration than rehydration \((p=0.03)\).

However, there was no difference when comparing its ability to detect volume changes during fluid administration to euhydrated animals (Experiment 1) versus dehydrated animals (Experiment 2, rehydration phase).

Figures 6, 7, and 8 show Bland-Altman plots for the isotonic crystalloid expansion of euolemic horses, the furosemide-induced dehydration, and the isotonic crystalloid rehydration of dehydrated horses respectively, using \( \text{ECFV}_{\text{MF-BIA}}(t) \). The 95% limits of agreement for MF-BIA detection of isotonic crystalloid expansion to euolemic horses are \((-2.1 \text{ to } +13.1 \text{L})\); for furosemide induced dehydration are \((-7.7 \text{L to } +1.5 \text{L})\); and for rehydration with an isotonic crystalloid are \((-6.0 \text{L to } +6.2 \text{L})\). For all three groups combined, the 95% limits of agreement are \((-8.8 \text{ to } +10 \text{L})\). Regression analysis of MF-BIA ERROR\( \text{ECFV}(t) \) with \( \Delta V(t) \) identified a statistically significant association during isotonic crystalloid infusion to euhydrated horses \((p<0.005, R^2=0.5)\) and during isotonic crystalloid infusions to dehydrated horses \((p=0.003, R^2=.43)\), suggesting that the error became relatively larger as the volume of fluid shift increased. However, we did not identify an association during furosemide-induced dehydration \((p=0.06, R^2=0.26)\).
DISCUSSION

This is the first study to compare the ability of MF-BIA to predict volume changes during dehydration, crystalloid expansion to euhydrated patients, and crystalloid expansion to dehydrated patients in horses. Isotonic expansion of the ECFV was detected well using the MF-BIA, and there was no difference in accuracy of MF-BIA to detect changes in fluid volume when administering crystalloids to euhydrated versus dehydrated horses. As expected with rapid fluid administration, the ECFV was expanded immediately and for up to 1 hour post-administration.

MF-BIA was better at predicting fluid loss (dehydration) than fluid administration. The ECFV was decreased by 1 hour post-administration of furosemide, and for up to 4 hours post as would be expected in horses administered diuretics and withheld from water. These are important findings, and they suggest that MF-BIA will be clinically useful in evaluating both dehydrated horses and those receiving fluid therapy, although it may be slightly more accurate during the initial evaluation of dehydrated horses rather than during volume replacement therapy.

The inability of MF-BIA to predict changes in ECFV due to acute blood loss and blood administration is a previously unreported finding, but may not be entirely unexpected. This may be due to the relatively small volume of blood (approximately 20% of estimated blood volume) removed and readministered. The 16 mL/kg change in blood volume (or only 10.4 ml/kg change in plasma volume) likely represents less than 5% of the total ECFV. The experiment would therefore need to be repeated with larger volumes of blood loss in order to evaluate its ability with more clinically significant hemorrhage. Another hypothesis for the lack of blood loss detection is that changes not
affecting the interstitial volume, such as those restricted to the vascular volume, may be more difficult to detect using MF-BIA. It would be helpful to remove a volume of blood and subsequently monitor the horses with MF-BIA for a longer time period than the 30 minute period in our study. This would aid in determining whether there was a decrease in BIA-predicted ECFV as fluid is drawn from the interstitial compartment into the vascular space as occurs after hemorrhage. MF-BIA consistently underestimated both contraction and expansion of the ECFV in this study. This underestimation of changes in ECFV was consistent throughout the study, which suggests it may also occur in the clinical setting. For the purposes of making treatment decisions, it is important to know that the technology typically slightly underestimates the true change in volume in horses. However, a meta-analysis addressing this question in people did not identify this same bias. The fluid expansion models used in this study primarily affected the ECFV. These were selected because of the difficulty in measuring changes in the ECFV, ICFV, and TBW concurrently using other techniques, such as dilution indicators. Despite not studying changes in the ICFV directly, MF-BIA correctly predicted that the fluid changes were limited to the ECFV, as would be expected with isotonic fluid administration. There was a statistically significant decrease in the volume of the ICFV at the end of the rehydration phase of Experiment 2. Because the horses were rehydrated with isotonic saline (0.9 %) solution, which is slightly hypertonic (308 mOsm/L) relative to the reported osmolarity for equine ECF (279-296 mOsm/L), it is possible that there was a small shift from ICFV to ECFV. This may explain the small decrease detected in ICFV in our study, although additional research is required to fully evaluate this hypothesis.
This study did not measure initial TBW and ECFV using a “gold standard” technique, such as dilution indicators. However, measurement of TBW and ECFV using MF-BIA has already been described in horses. The goal of this study was to evaluate the ability of BIA to detect changes in fluid volumes, not absolute volumes, and therefore the relative loss or gain of fluid was more important than the exact starting volume. Comparing MF-BIA predicted changes to the amount of fluid lost or administered and to weight changes has been used in a similar manner to validate the technology in people. Bioelectrical impedance analysis, and specifically MF-BIA, has a potentially wide application in the critical care setting, but defining its strengths and weaknesses under different specific physiological states requires further evaluation. This study demonstrated that MF-BIA can detect changes in ECFV and TBW associated with dehydration and isotonic crystalloid expansion. However, MF-BIA may not detect changes in ECFV and TBW associated with modest acute blood loss or administration (16 mL/kg volume; approximately 20% of blood volume). MF-BIA may therefore be useful in detecting dehydration and for monitoring fluid balance during crystalloid administration in horses in the clinical setting.
Table 1: ECFV, ICFV, and TBW predicted by MF-BIA prior to infusion, end infusion, 1 hr post-infusion, and 2 hr post-infusion of a 40ml/kg isotonic crystalloid to over 30 minutes. Values are listed as median (range).

<table>
<thead>
<tr>
<th>Volume (L)</th>
<th>Pre-infusion</th>
<th>End-infusion</th>
<th>1hr post-infusion</th>
<th>2hr post-infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECFV (BIA)</td>
<td>112.2 (102.8 : 118.9)</td>
<td>124.3* (112.6 : 133.6)</td>
<td>118* (110.9 : 131.2)</td>
<td>116.5 (110.9 : 128.9)</td>
</tr>
<tr>
<td>ICFV (BIA)</td>
<td>230.7 (218 : 286.6)</td>
<td>233.6 (216.7 : 289.7)</td>
<td>233.2 (210.9 : 294)</td>
<td>239.2 (211.5 : 289)</td>
</tr>
<tr>
<td>TBW (BIA)</td>
<td>343 (330 : 404.1)</td>
<td>359.2* (330.3 : 415)</td>
<td>351.5 (324 : 412)</td>
<td>352.6 (328 : 406.3)</td>
</tr>
</tbody>
</table>

* indicates a statistically significant difference from the pre-infusion value (p<0.05)

Table 2: Change from baseline in MF-BIA-predicted ECFV, ICFV and TBW and the measured net change in volume immediately after infusion, 1 hr after infusion and 2 hr after infusion of a 40ml/kg isotonic crystalloid to euvolemic horses over 30 minutes. Values are given as median (range).

<table>
<thead>
<tr>
<th>Volume (L)</th>
<th>Change at end infusion</th>
<th>Change 1hr post-infusion</th>
<th>Change 2hr post-infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECFV (BIA)</td>
<td>9.8 (7.8 : 16.1)</td>
<td>6.3 (0.5 : 12.3)</td>
<td>4.5 (-0.2 : 10)</td>
</tr>
<tr>
<td>TBW (BIA)</td>
<td>11 (-2.2 : 31)</td>
<td>4.2 (-8.5 : 18)</td>
<td>5.1 (-2 : 20.1)</td>
</tr>
<tr>
<td>Real Change</td>
<td>17.1 (16.2 : 21.1)</td>
<td>10 (3.9 : 15.2)</td>
<td>8.2 (1.7 : 11.5)</td>
</tr>
</tbody>
</table>

Table 3: MF-BIA predicted ECFV, ICFV, and TBW during furosemide (1mg/kg) induced dehydration to euvolemic horses. Values are given as median (range).

<table>
<thead>
<tr>
<th>Volume (L)</th>
<th>Pre-dehydration</th>
<th>1 Hour dehydration</th>
<th>2 Hour dehydration</th>
<th>3 Hour dehydration</th>
<th>4 Hour dehydration</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECFV (BIA)</td>
<td>114.4 (100.8 : 126.9)</td>
<td>106.6* (94.4 : 118.9)</td>
<td>104.3 (96.9 : 119.1)</td>
<td>104.3 (96.5 : 119.2)</td>
<td>103.5* (96.1 : 118.1)</td>
</tr>
<tr>
<td>ICFV (BIA)</td>
<td>244.4 (216 : 295.3)</td>
<td>240 (216.2 : 302.2)</td>
<td>249 (213.7 : 297.2)</td>
<td>246.1 (209.7 : 295.3)</td>
<td>242.7 (208.8 : 298.7)</td>
</tr>
<tr>
<td>TBW (BIA)</td>
<td>351.2 (316.7 : 420.4)</td>
<td>343.6 (310.6 : 421.1)</td>
<td>349.3 (310.6 : 416.3)</td>
<td>346.6* (306.3 : 414.5)</td>
<td>347.3 (304.9 : 416.7)</td>
</tr>
</tbody>
</table>

* Indicates a statistically significant difference from the pre-dehydration values (p<0.05)
Table 4: Change in baseline from MF-BIA predicted ECFV, ICFV and TBW and the measured net change in volume during furosemide (1 mg/kg) induced dehydration in euvoletic horses. Values are given as median (range).

<table>
<thead>
<tr>
<th>Volume (L)</th>
<th>1 hour dehydration</th>
<th>2 hour dehydration</th>
<th>3 hour dehydration</th>
<th>4 hour dehydration</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECFV</td>
<td>-7.4 (-11.4 : -2.1)</td>
<td>-8.2 (-11.9 : -2.8)</td>
<td>-8.1 (-13 : -3.2)</td>
<td>-9.1 (-14.2 : -3)</td>
</tr>
<tr>
<td>ICFV</td>
<td>2.5* (-9.1 : 6.9)</td>
<td>-1* (-6.7 : 15.9)</td>
<td>-1.0* (-12.7 : 16.4)</td>
<td>2.8* (-14.8 : 16.8)</td>
</tr>
<tr>
<td>TBW</td>
<td>-6.1 (-13.3 : 0.8)</td>
<td>-7 (-16.9 : 5.5)</td>
<td>-9.2 (-19 : 6.5)</td>
<td>-4.5 (-29 : 6)</td>
</tr>
<tr>
<td>Real Change</td>
<td>-9.9 (-12.8 : -7.3)</td>
<td>-10.8 (-14.7 : -9)</td>
<td>-11.2 (-14.8 : -9.6)</td>
<td>-11.5 (-15.3 : -9.9)</td>
</tr>
</tbody>
</table>

* indicates a statistically significant difference from the real change in volume (p<0.05)

Table 5: MF-BIA predicted ECFV, ICFV, and TBW during rehydration with 40 ml/kg of an isotonic crystalloid administered to dehydrated horses over two hours. Values are given as median (range).

<table>
<thead>
<tr>
<th>Volume (L)</th>
<th>Pre-rehydration</th>
<th>1 Hour rehydration</th>
<th>2 Hour rehydration</th>
<th>3 Hour rehydration</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECFV (BIA)</td>
<td>103.5 (96.1 : 118.1)</td>
<td>112.6 (103.7 : 126.3)</td>
<td>120.1* (108.3 : 133.4)</td>
<td>118.2* (106.1 : 131.2)</td>
</tr>
<tr>
<td>ICFV (BIA)</td>
<td>242.7 (208.8 : 304.9)</td>
<td>240.0 (210.7 : 296.3)</td>
<td>237.1* (209.7 : 295.5)</td>
<td>243 (210.3 : 295.6)</td>
</tr>
<tr>
<td>TBW (BIA)</td>
<td>347.3 (304.9 : 416.7)</td>
<td>348.3 (314.4 : 422.6)</td>
<td>352.7* (319.8 : 428.9)</td>
<td>359.8* (320.7 : 426.8)</td>
</tr>
</tbody>
</table>

* indicates a statistically significant difference from the pre-rehydration values.

Table 6: Change in baseline from MF-BIA predicted ECFV, ICFV and TBW and the measured net change in volume with 40ml/kg of an isotonic crystalloid to dehydrated horses over two hours. Values are given as median (range).

<table>
<thead>
<tr>
<th>Volume (L)</th>
<th>1 Hour Rehydration</th>
<th>2 Hour Rehydration</th>
<th>3 Hour Rehydration</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECFV (BIA)</td>
<td>-0.25 (-6.3 : 2.9)</td>
<td>6.2 (0.5 : 9.3)</td>
<td>3.8 (-2.4 : 9.6)</td>
</tr>
<tr>
<td>ICFV (BIA)</td>
<td>-0.5 (-18.3 : 12.5)</td>
<td>-3.0* (-20.8 : 9.5)</td>
<td>3 (-12.2 : 18)</td>
</tr>
<tr>
<td>TBW (BIA)</td>
<td>-0.6 (-24.6 : 10.7)</td>
<td>4.5 (-20.3 : 15.1)</td>
<td>6.2 (-14.6 : 20.7)</td>
</tr>
<tr>
<td>Real Change</td>
<td>-1.7 (-6 : -0.3)</td>
<td>7.9 (1 : 9.1)</td>
<td>6.2 (-2 : 8.6)</td>
</tr>
</tbody>
</table>

* indicates a statistically significant difference from the real change (p<0.05).
Table 7: MF-BIA predicted ECFV, ICFV, and TBW during 16ml/kg blood loss and 16ml/kg blood administration. Values are given as median (range).

<table>
<thead>
<tr>
<th>Volume (L)</th>
<th>Baseline</th>
<th>Blood Loss</th>
<th>Blood re-administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECFV (BIA)</td>
<td>113.9 (108.6 : 124.4)</td>
<td>111.5 (107.8 : 124.3)</td>
<td>113.2 (108.6 : 123.9)</td>
</tr>
<tr>
<td>ICFV (BIA)</td>
<td>250.2 (224.6 : 317.4)</td>
<td>247.5 (216.9 : 309.9)</td>
<td>244.9 (220.5 : 299.7)</td>
</tr>
<tr>
<td>TBW (BIA)</td>
<td>364.3 (333.2 : 441.8)</td>
<td>359.9 (324.7 : 434.2)</td>
<td>359 (329.1 : 423.6)</td>
</tr>
</tbody>
</table>

No statistically significant changes from baseline.

Table 8: Change from baseline in MF-BIA predicted ECFV, ICFV and TBW after a 16ml/kg blood loss and a 16ml/kg blood administration. Values are given as median (range).

<table>
<thead>
<tr>
<th>Volume (L)</th>
<th>Blood Loss</th>
<th>Blood re-administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECFV (BIA)</td>
<td>-1.2 (-4.7 : 0.1)</td>
<td>0.5 (-3.6 : 2.2)</td>
</tr>
<tr>
<td>ICFV (BIA)</td>
<td>-7.6 (-15.3 : 7)</td>
<td>-9 (-17.7 : 11)</td>
</tr>
<tr>
<td>TBW (BIA)</td>
<td>-8.1 (-16.8 : 7.1)</td>
<td>-8.4 (-19.2 : 13.2)</td>
</tr>
<tr>
<td>Real Change</td>
<td>-9.2 (-10 : -7.9)</td>
<td>0.4 (-0.4 : 1.3)</td>
</tr>
</tbody>
</table>

No statistically significant differences detected.
Figure 1: Graph of the median change in volume as compared to the MF-BIA predicted changes in ECFV, ICFV and TBW during crystalloid infusion.

The infusion (40ml/kg) of an isotonic crystalloid was started at time zero and finished at 30 minutes.

Figure 2: Graph of the median change in volume as compared to the MF-BIA predicted changes in ECFV, ICFV, and TBW during dehydration (furosemide) and rehydration with an isotonic crystalloid.

Furosemide was administered at time zero and the infusion (40ml/kg) was started at 300 minutes.
Figure 3: Comparison of the median values of the measured net change in volume with the MF-BIA predicted changes in ECFV, ICFV, and TBW during blood loss and blood administration.

The blood removal was started at time zero and the blood administration was begun at approximately sixty minutes. However, it was not possible to keep the rate exactly the same for each horse, and therefore the times are approximate.
Figure 4: The measured change in volume calculated by infused volume minus urinary losses (i.e., estimate of net volume change) as compared with the MF-BIA predicted change in TBW.

Figure 5: The measured change in volume ($\Delta V_T$) compared with the MF-BIA predicted change in ECFV (EFCV$_{MF-BIA*T}$).
Figure 6: Bland Altman plot comparing the change in ECFV ($\Delta V_T$) with the error between the measured net change and the MF-BIA predicted change ($\text{MF-BIA ERROR}_{\text{ECFV(t)}}$) during crystalloid infusion to euhydrated horses.

Figure 7: Bland Altman plot comparing the change in ECFV ($\Delta V_T$) with the error between the measured net change and the MF-BIA predicted change ($\text{MF-BIA ERROR}_{\text{ECFV(t)}}$) during furosemide induced dehydration.
Figure 8: Bland Altman plot comparing the change in ECFV ($\Delta V_T$) with the error between the measured net change and the MF-BIA predicted change ($\text{MF-BIA ERROR}_{\text{ECFV}(t)}$) during rehydration following furosemide dehydration.

Comparison of the error between MF-BIA predicted change in ECFV with the real change in ECFV during crystalloid infusion to dehydrated horses.

Real change in volume (L)

Error (L)
Footnotes

Angiocath; Becton-Dickinson and Co.; Franklin Lakes, NJ

Silicone Coated Foley Catheter; Kendall; Mansfield MA

Grass platinum, tetrapolar, subdermal 27-gauge needle electrodes, 122 cm, Astro-Med Inc, West Warwick, RI

Hydra ECF/ICF bioimpedance analyzer, Model 4200, Xitron Technologies, San Diego, CA

Sklar Compressor Unit (model 100-15) J Sklar Manufacturing; Sorenson Research Co, Inc, Long Island City NY

Anticoagulant Citrate Dextrose Solution, Medsep Corp, Covina CA
References


