A Pilot Multi-Center Examination of Near Infra Red Spectroscopy (NIRS) in the evaluation of Hemoglobin (Hb) Levels in Trauma Patients Receiving Blood Transfusions

KEY WORDS: Near Infra Red Spectroscopy, Trauma patients, and Blood transfusion

ABSTRACT

In the traumatically injured patient population, repeated blood draws and analysis for hemoglobin concentration (Hb) are widely utilized to evaluate blood loss.The objective of this study is to compare a prototype near infrared spectroscopy (NIRS) device designed to non-invasively monitor peripheral hemoglobin concentration to the standard blood drawn hemoglobin values in intensive care patients receiving a red blood cell transfusion. The study was set in 4 Surgical Intensive Care Units level 1 trauma centers in Illinois Thirteen (N=13), 5 female and 8 male (ages:19-55) traumatically injured patients admitted to the surgical intensive care units of four Chicago Land level one trauma centers and requiring a red blood cell transfusion. Non-invasive monitoring of hemoglobin was conducted via a light emitting spectroscopy probe placed on the patient's thenar eminence via an adhesive cover, prior to the initiation of red blood cell transfusion. The main objective of this study was the comparison of 13 patients' (N=13) blood drawn hemoglobin values pre (#1Bd Hb) and post-transfusion (#2 Bld Hb) to those values obtained (#1THI& #2THI) peripherally via a non-invasive spectroscopy (NIRS) technique known as a "Tissue Hemoglobin Index" (THI). Pre-transfusion comparison produced ($R=0.587$, $p=0.035$), ($R^2=0.345$), paired T-test ($p=0.705$). Post-transfusion ($R=0.550$, $p=0.051$), ($R^2=0.303$), paired T-test ($p=0.947$). Both the pre- and post-transfusion comparisons produced positive correlations with significant p-values, though both coefficients of determination were (<50%), which indicates that a discrepancy between the 2 values exists. Though, when analyzed utilizing a paired T-test no statistically significant difference was found between the two techniques.

Secondary analysis compared the changes in values (increases) resulting from the transfusion of red blood cells, ($R=0.380$, $p=0.200$), ($R^2=0.145$), paired T-test ($p=0.700$). This comparison did not produce a statistically significant correlation although the paired T-test

produced a p-value which indicated that no statistically significant difference existed between the two methodologies of hemoglobin determination.

Overall the pilot study produced encouraging results with respect to the ability of NIRS to non-invasively monitor hemoglobin concentration though with some deviation from traditional blood drawn values. In this small pilot study several confounding factors may have played a role in these deviations and were not specifically addressed in the study design. Hemoglobin values can be especially useful in cases where red blood cell transfusion, fluid resuscitation, or surgical intervention is required. However, current methods available for measuring Hb are invasive (requiring blood sampling) and are intermittent in nature. A device capable of continuous, real time, non-invasive monitoring of Hb would improve recognition of blood loss and provide a means of assessing the oxygen carrying capacity of blood during ongoing resuscitation efforts.

INTRODUCTION

In the traumatically injured patient population, repeated blood draws and analysis for hemoglobin concentration (Hb) are widely utilized to evaluate blood loss and hemodynamic state. Hemoglobin values can be especially useful in cases where red blood cell transfusion, fluid resuscitation or surgical intervention is require; however, current methods available for measuring (Hb) are invasive (requiring blood sampling) and are intermittent in nature. A device capable of continuous, real time, non-invasive monitoring of (Hb) would improve recognition of blood loss and provide a means of assessing the oxygen carrying capacity of blood during ongoing resuscitation efforts.

The use of non-invasive near infrared spectroscopy (NIRS) has been used in the research field for several years, and has recently begun to see a wider application in the clinical arena [1,2,3,4,5,6] NIRS uses the ability of near infrared light to pass through biologic materials such as skin and muscle with less scattering than light of shorter wavelengths. In this process a known quantity of light is passed through a specific area of tissue. The amount of light recovered is dependent upon the amount of light absorbed by chromophores (iron atoms in hemoglobin) present in the tissue of interest and the amount of light scatter caused by the tissue. Overall the amount of scatter may be considered constant for a specific optical arrangement in a known tissue. [7,8,9]

The Beer-Lambert law is the mathematical principle used to describe light absorption and the properties of the material through which the light is traveling. Because the light absorbance and extinction coefficients of oxyhemoglobin and deoxyhemoglohbin are different, Beer's law may be used to quantify the relative concentrations of each in human tissue.[10,11,12,13]

This technology has been employed for the evaluation of hemoglobin concentration in several research studies using a variety of anatomical sites with differing degrees of accuracy when compared to blood drawn hemoglobin values.[14,15,16,17,18] Factors that appear to contribute to these variances in Hb values are choice of anatomical site, and the variability in blood flow volume that exists at different anatomical locations.

In situations involving hypovolemia, blood loss, and shock, the sympathetic nervous system compensates for blood loss through a sequential vasoconstriction beginning at the periphery in order to preserve perfusion to vital organs.[19,20,21] Because the extremities are among the first anatomical sites to experience this compensatory vasoconstric-

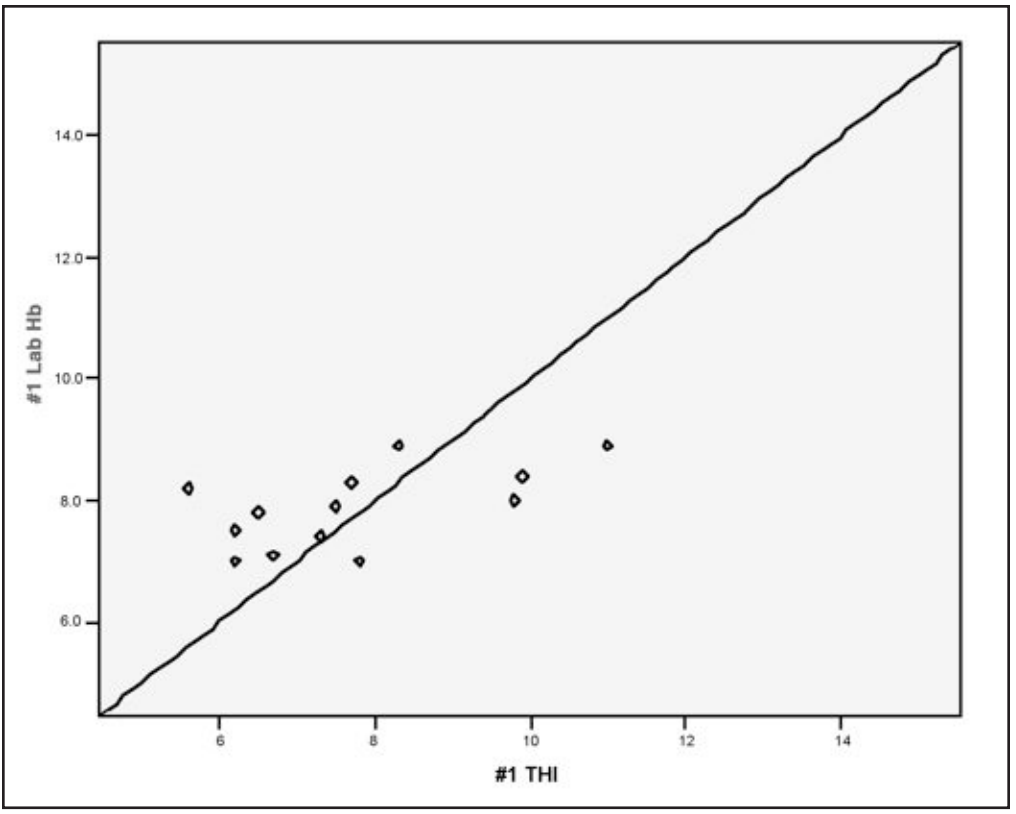

Figure 1. This scatter plot represents the pre-transfusion blood drawn hemoglobin values (#1 Lab Hb) plotted against the pre-transfusion values obtained via near-infra spectroscopy (#1 THI). The diagonal line in the graph represents an exact one to one relationship between the two types of values.

tion, the periphery is a logical site for the placement of a sensor intended to detect early subtle variations in hemoglobin concentration. In 2 recent multi-site studies, NIRS monitoring at the thenar eminence was successfully utilized in the assessment of regional peripheral muscle oxygenation (StO2) and this parameters relationship to the severity of shock and organ dysfunction in trauma patients.[22,23] Other advantages of utilizing the thenar eminence include easy identification and access, and the relative consistency of the thickness of tissue from person to person even, in cases of sepsis and edema.[24]

This multi-site pilot study compares standard clinical laboratory hemoglobin levels pre- and post-transfusion to values obtained via a prototype near infrared spectrometer (NIRS) that employs experimental software to derive a peripheral hemoglobin concentration, or Tissue Hemoglobin Index (THI) at the thenar eminence.[25] This pilot study seeks to collect preliminary data on the relationship between the two methodologies for the purpose of exploring the potential of NIRS to perform additional non-invasive monitoring in the critically ill patient population. This study utilizes NIRS readings obtained from traumatically injured patients at four level one trauma centers which are compared to standard blood drawn hemoglobin values obtained from their respective clinical laboratories before and after the transfusion of two units of packed red blood cells (PRBC).

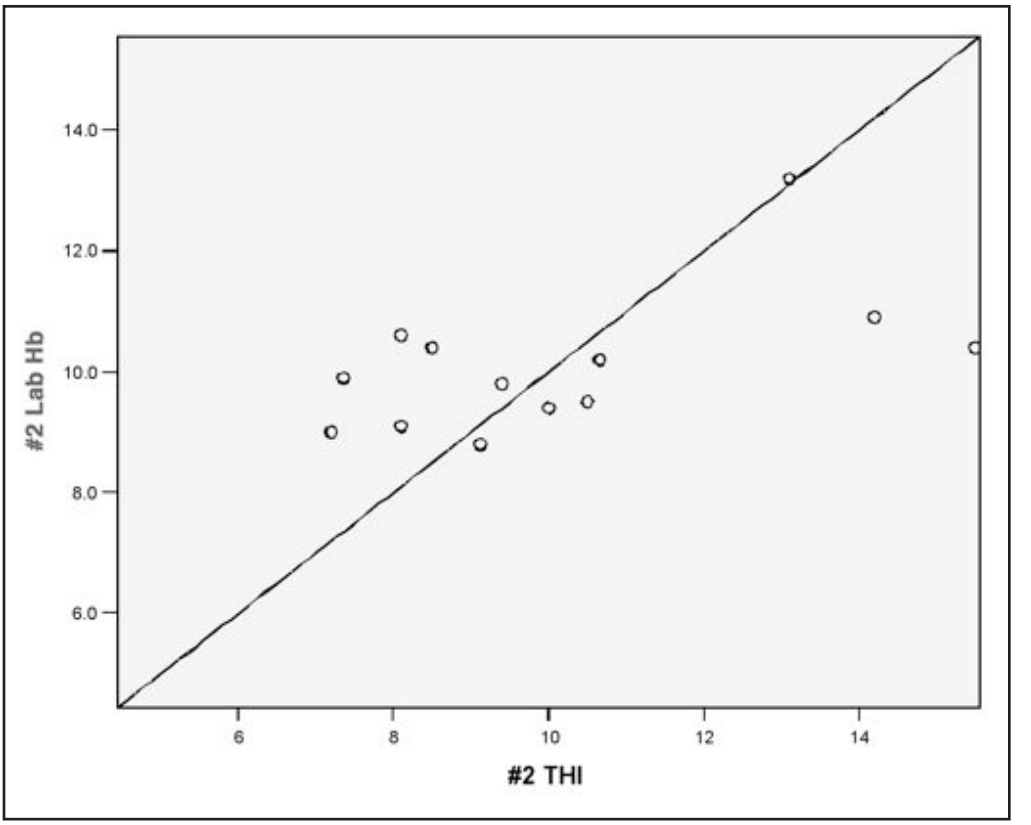

Figure 2. This scatter plot represents the post-transfusion blood drawn hemoglobin values (#2 Lab Hb) plotted against the post-transfusion values obtained via near-infra spectroscopy (#2 THI). The diagonal line in the graph represents an exact one to one relationship between the two types of values.

MATERIALS AND METHODS

The prototype tissue spectrometer utilized in this pilot study was the In Spectra Model 325™ Hutchinson Technologies Inc., Bio Measurement Division, Hutchinson MN. This spectrometer utilizes three light wavelengths (680, 720, 760 nm) and the absorbance of each with respect to hemoglobin to derive a relative value of the amount of hemoglobin flowing through the thenar muscle capillary bed.[25] This device is self-calibrating, though a standardized control device was provided by the company in order to assure that the device was operating within the normal parameters established by the manufacturer.

The blood drawn hemoglobin values obtained for comparison and statistical analysis were performed within the clinical laboratories of the 4 tertiary care centers. The calibration and standards established at each of these laboratories are based on a standard deviation of 0.2 g/dL of hemoglobin, with 2 standard deviations being an acceptable variance from sample to sample.

A study protocol was submitted and approved by the Advocate Health Care Institutional Review Board. It was then implemented at 4 state designated level 1 trauma centers—Advocate Christ Medical Center, Oak Lawn IL; Advocate Good Samaritan Hospital, Downers Grove IL; Advocate Illinois Masonic Medical Center, Chicago IL; and Advocate Lutheran General Hospital, Park Ridge IL.

The study protocol inclusion criteria stipulated subjects who were trauma

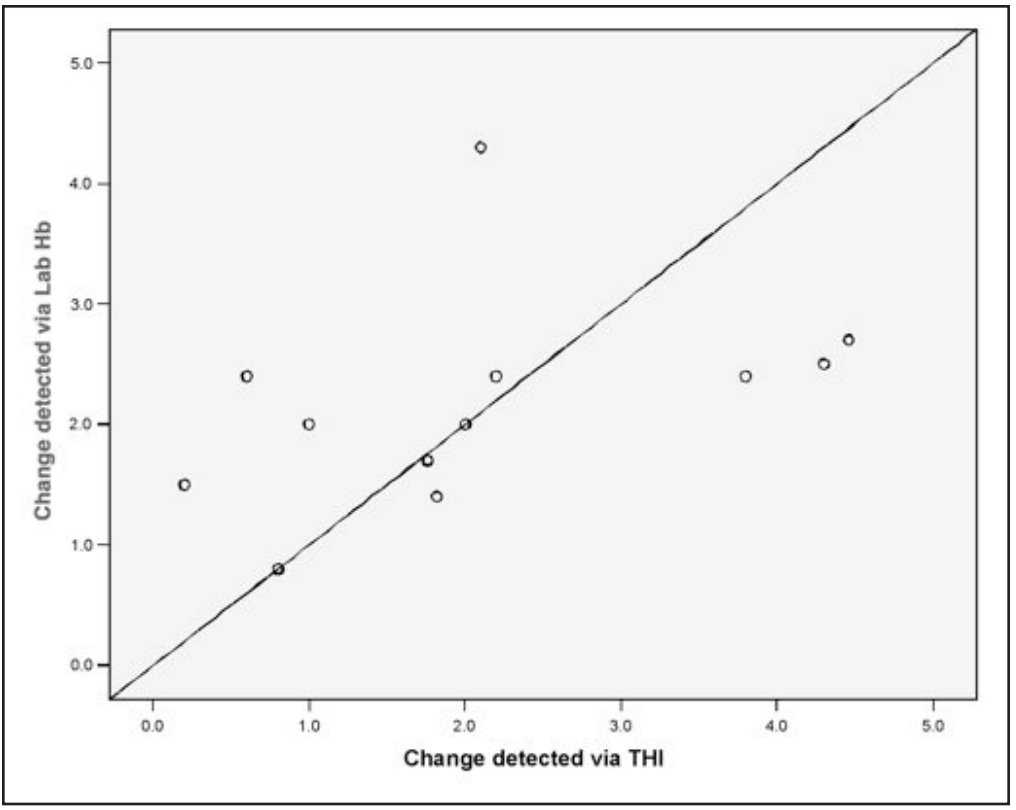

Figure 3. This scatter plot represents the changes in THI detected via spectroscopy (Change detected via THI) plotted against the changes in Hb value detected by the blood drawn Hb values (Change detected via Lab Hb) plotted against each other in a 1:1 scale with the diagonal line representing an exact one to one relationship.

patients, male or female, 18 years of age or older and admitted to the Surgical Intensive Care Unit (SICU) and medically determined to be hemodynamically stable, with the exception of having a subnormal hemoglobin value and requiring a red blood cell transfusion. Eight males and 5 females (N=13) 19 and 55 years of age (mean age 41 yrs) met all inclusion/exclusion criteria for the study. Hemodynamically unstable patients were excluded from the study to avoid the compounding of variables which are beyond the scope of this pilot study.

Subjects in the SICU were screened by an attending physician and hemoglobin values evaluated based on the most current laboratory results of the day. Upon determination by the attending physician that the patient required a transfusion of 2 units of packed red blood cells (PRBC) and was an appropriate subject for the study (stable multi-trauma patients), informed consent was obtained and the subject enrolled into the study.

The initial blood hemoglobin values used to determine the need for a transfusion was documented and designated (#1Bld.Hb.). The spectrometer probe was then placed on the available thenar eminence (without proximal catheter) via an adhesive polyethylene cover prior to the initiation of blood transfusion. An initial pre-transfusion spectroscopy value (#1 THI) was documented. Two units of packed red blood cells were then transfused via an infusion pump with a mean infusion rate of 239 ml/Hr

Table 1. Values obtained for thirteen subjects (N=13) standard blood drawn hemoglobin values pre (#1 Bld Hb) and post-transfusion (#2 Bld Hb), and those values obtained by near infrared spectroscopy pre (#1THI) and post-transfusion (#2 THI). The differences between values obtained by each method are also listed for the pre-transfusion data (Diff (#1THI - #1 Bld Hb)) and for the post-transfusion data (Diff (#2 THI - #2 Bld Hb)).

Subject	#1 Bld Hb	#1 THI	Diff 2 (#1THI-#1 BLD HB)	#2 Bld HB	#2 THI	Diff(#2 THI - #2 Bld Hb)
47 male	8.2	5.6	-2.6	9.9	7.4	-2.5
19 male	7	6.2	-0.8	9	7.2	-1.8
47 female	7.5	6.2	-1.3	10.2	10.7	0.5
55 male	7.8	6.5	-1.3	9.8	9.4	-0.4
39 female	7.1	6.7	-0.4	9.5	10.5	1
40 female	7.4	7.3	-0.1	8.8	9.1	0.3
37 female	7.9	7.5	-0.4	10.6	8.1	-2.5
49 male	8.3	7.7	-0.6	9.1	8.1	-1
37 female	7	7.8	-0.8	9.4	10	0.6
55 male	8.9	8.3	-0.6	10.4	8.5	-1.9
23 male	8	9.8	1.8	10.4	15.5	5.1
47 male	8.4	9.9	1.5	10.9	14.2	3.3
39 male	8.9	11	2.1	3.2	13.1	-0.1

and a mean volume of 350ml/unit PRBC. The time of transfusion completion and a post-transfusion follow up blood hemoglobin value (#2Bld.Hb.) and post-transfusion spectroscopy value (#2 THI) were documented.

For statistical analysis the mean of the 13 blood drawn hemoglobin values were compared to the mean of the 13 values obtained via spectroscopy pre and post-transfusion utilizing Pearson Correlation Coefficients (R), Coefficients of Determination (R^2), and paired T-tests. Also analyzed were the changes in values occurring from pre-transfusion to post-transfusion for the laboratory Hb values (¢ Chg. Bld Hb) and those obtained via NIRS (¢ Chg. THI) using the same statistical tests. All statistical calculations were performed with a 95% confidence interval (· = 0.05) and a two-tailed test.

RESULTS

During the pilot study period, 13 surgical intensive care patients determined to require a red blood cell transfusion were recruited from 4 level 1 trauma centers. The main objective of the study was to compare the blood drawn hemoglobin values to those values obtained via non-invasive spectroscopy (NIRS) known as a "Tissue Hemoglobin Index" (THI), before and after transfusion of 2 units of PRBC. Additionally, an analysis of the changes in values occurring as a result of the transfusion of two units of PRBC was performed.

Pre-transfusion comparison of the blood drawn hemoglobin values (#1 Bld.Hb) compared to the Tissue Hemoglobin Index (#1 THI), (Fig.1, Table 1) produced a Pearson Correlation Coefficient of R=0.587 (p = 0.035) and a Coefficient of Determination of R^2=0.345 and a variance between groups of 1.49. The paired T-test revealed a p-value = 0.705 indicating no statistically significant difference between the 2 mean values.

Analysis of the post-transfusion blood drawn hemoglobin value (#2

Bld.Hb) compared to the post-transfusion Tissue Hemoglobin Index (#2 THI), (Fig.2, Table1) produced an R=0.550 (p = 0.051) and an $R^2 = 0.303$ and a variance between groups of 3.95. The paired T-test post-transfusion produced a p-value = 0.947, again exhibiting no statistically significant difference between the two groups.

Comparison of the changes detected by the blood drawn hemoglobin (¢Chg.Bld.Hb) with respect to the changes obtained via NIRS (¢Chg.THI),(Fig.3), produced a variance between groups of 1.72 and an R=0.380 (p = 0.200) and an $R^2 = 0.145$ with no statistically significant correlation. The paired T-test resulted in a p-value = 0.700 indicating that no statistically significant difference existed between the 2 groups of measurement.

The comparison between standard blood drawn hemoglobin values obtained from a clinical laboratory and those values obtained through the use of the In Spectra 325™ tissue spectrometer revealed statistically significant positive correlations between the 2 methodologies though these correlations are not particularly strong($R^2<0.5$). NIRS did produce values approximating those obtained via the standard blood draw and displayed a quantitative increase with the transfusion of additional red blood cells (Table.1). The values obtained via spectroscopy varied for 2 of the subjects by as much as +/- 2.6 in a single subject for the pre-transfusion data and as much as +/- 5.1 for 1 subject in the post-transfusion data. These two variations in readings do not seem to coincide with the other 11 subjects or the means calculated for the group, though several possible factors may have contributed to these differences in readings.

DISCUSSION

Due to the pilot nature of this study and the fact that it represents the initial use of a prototype device and algorithm, several limitations must be noted with regard to possible confounding factors that were not addressed in the study design. Foremost for consideration is the small sample size. Because this study is an initial investigation into a relatively unknown parameter using a prototype device, a traditionally powered study could not be justified. Additionally invasive measures such as serial blood draws were deemed an unnecessary risk to the patient for the purposes of a pilot study. Similarly, additional blood draws, which directly coincided with probe placement and removal, were not obtained. This may have been a contributing factor in some of the variations in readings. Another limitation to the overall pilot nature of the study would be the lack of stratification into subgroups for the detailed analysis of components such as injury severity and active medications in use over the data collection period. In the design phase it was noted that a device intended for a broad heterogeneous clinical utilization would need to provide useful parameters across a broader population if it was to be a truly useful endeavor.

These variables are being considered for further evaluation in the development of a larger, more extensive study in order to generate more generally applicable results and improve upon the initial spectroscopy algorithm utilized. The several confounding factors not addressed in this pilot study may have compounded the variability of the spectrometer readings. Additionally, a small amount of drift both above and below the blood drawn hemoglobin values was noted in the spectroscopy values during the study. This drift may have also contributed to some of the variances in values. This issue is being examined and may have been caused by the prototype nature of the device. In this first genera-

tion device, the sensitivity as well as the frequency of readings was set to a maximum degree. This extreme sensitivity has the potential to produce some unexpected variations. This issue is under current evaluation as well as the algorithm that may benefit from a mechanism which considers more than a single reading in its determination of hemoglobin concentration.

With these limitations in mind, the study appears to have produced relevant correlations and statistics between the blood drawn hemoglobin values and those readings obtained from the spectroscopy device, with the exception of a pre-transfusion deviation in values for 1 subject and a post-transfusion deviation for another. For the purpose of establishing NIRS as a valid useful clinical tool with respect to hemoglobin concentration, a broader more detailed research study would be required before any clinically significant claims could be made. These issues require further evaluation in a larger group with more possible confounding variables accounted for in order to make a scientific assumption with respect to which of the factors play a role in variation and those which are of minor relevance.

CONCLUSION

In the final analysis of the data produced in this pilot study, it is apparent that in order to make any specific recommendations or inferences about the device's accuracy and/or predictability of hemoglobin, concentration sample size needs to be expanded and more variables examined. At the same time, it also appears that this pilot study has in fact identified several potentially confounding issues as well as laying the rudimentary ground work for the next phase of evaluation. In comparison to other studies performed for the purpose of determining hemoglobin concentration, this study displays more variability in values[14,15] though its population is vastly different from healthy young individuals. Both the manufacturer and the researchers are currently developing a broader study incorporating the findings of this study to address and potentially answer some of the questions raised by this pilot. Should this technology continue to evolve for application in the critical care setting it may provide valuable additional information to the clinician.

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