EXPLORATORY ANALYSIS OF CARBON DIOXIDE LEVELS AND ULTRASOUND MEASURES OF THE EYE DURING ISS MISSIONS

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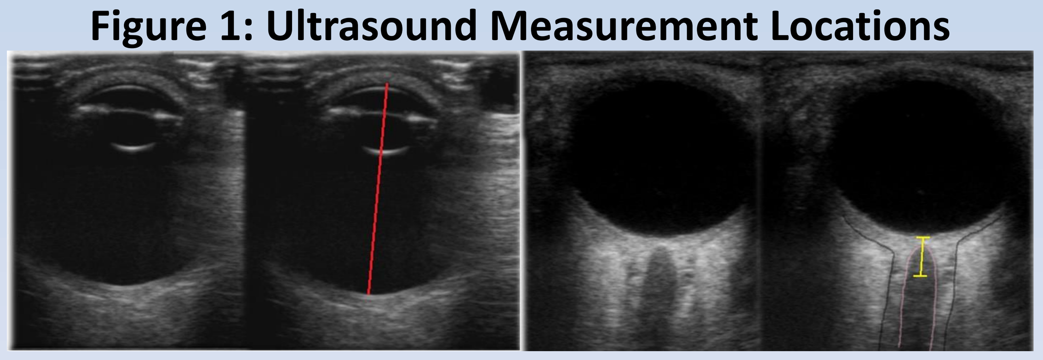
Background

Carbon dioxide (CO_2) levels on ISS have typically averaged 2.3 to 5.3 mm Hg, with large fluctuations occurring over periods of hours and days. CO_2 has effects on cerebral vascular tone, resulting in vasodilation and alteration of cerebral blood flow (CBF). Increased CBF leads to elevated intracranial pressure (ICP), which is a factor leading to visual disturbance, headaches, and other central nervous system symptoms. Ultrasound of the optic nerve provides a surrogate measurement of ICP. In-flight ultrasounds were implemented as an enhanced screening tool for the Visual Impairment/Intracranial Pressure (VIIP) Syndrome. This analysis examines the relationships between ambient CO_2 levels on ISS and ultrasound measures of the eye in an effort to understand how CO_2 may be associated with VIIP and to inform future analysis of inflight VIIP data.

Methods

Inflight ultrasound measurements of the eye were collected on flight days 30, 90, and R-30 (±7 days). These measurements include optic nerve diameter (OND), optic nerve sheath diameter (ONSD), and anterior-posterior (AP) diameter. OND and ONSD were measured in a standardized axial plane avoiding the anterior chamber of the eye. OND and ONSD are assessed at 3mm from the retinal interface. AP diameter was measured in the near-axial plane adjusted to pass through the corneal vertex and the optic nerve head. The actual measurement was made perpendicular to the plane of the iris to reflect the distance from the corneal surface to the surface of the retina in the macular region (Figure 1). Images were acquired with a multipurpose ultrasound system (ATL/Philips Medical Systems, WA, USA) prior to 2011. The vivid q ultrasound system (General Electric, USA) was implemented in 2012 for inflight examinations, also with 12 MHz linear array probes. Analysis was completed using the Synapse Cardiovascular DICOM analysis software tool (Fujifilm, USA).

Figure 1: Ultrasound Measurement Locations



CO_2 measurements were pulled directly from Operation Data Reduction Complex for the Lab and Node 3 Major Constituent Analyzers on ISS. CO_2 concentrations were recorded approximately every six or seven minutes. CO_2 measures between ultrasounds were summarized using standard time series class metrics in MATLAB including mean, standard deviation, variance, median, interquartile range, maximum, and minimum. Regression analyses were used to quantify relationships between the CO_2 metrics and ultrasound measures. Generalized estimating equations adjusted for the repeated measures between individuals and demographic variables were included (age, sex, time spent in microgravity, etc.). Table 1 describes the characteristics of the ISS USOS crewmembers, from Expeditions 19-32 (N=9) who were evaluated.

Table 1: Characteristics of Crewmembers Evaluated

Variables	Mean ± standard deviation
Males, %	77.8
Females, %	22.2
Mean age at test, in years	48.9 ± 5.4
Mean spaceflight duration to test, in days	132.1 ± 84.5
Mean number of tests per crewmember	4.0 ± 1.7

Results

As shown in Figure 2, there was a large time frame where CO_2 readings were removed due to sensor fault errors (see Limitations), from June 2011 to January 2012. After extensive cleaning of the CO_2 data, metrics for all of the data were calculated (Table 2). Preliminary analyses showed possible associations between variability measures of CO_2 and AP diameter (Figure 3), and average CO_2 exposure and ONSD (Figure 4). Adjustments for multiple comparisons were not made due to the exploratory nature of the analysis.

Figure 2: CO2 Level Readings on ISS

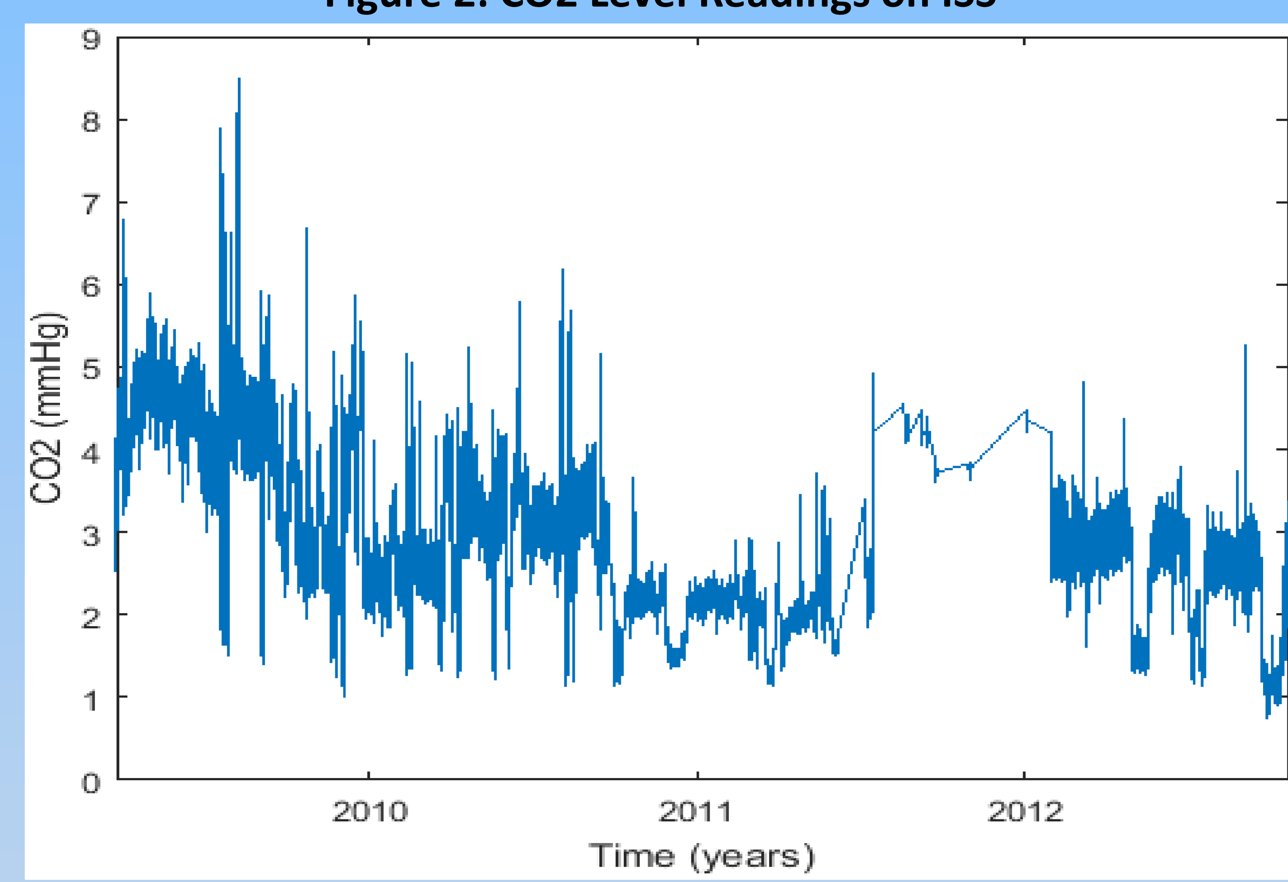
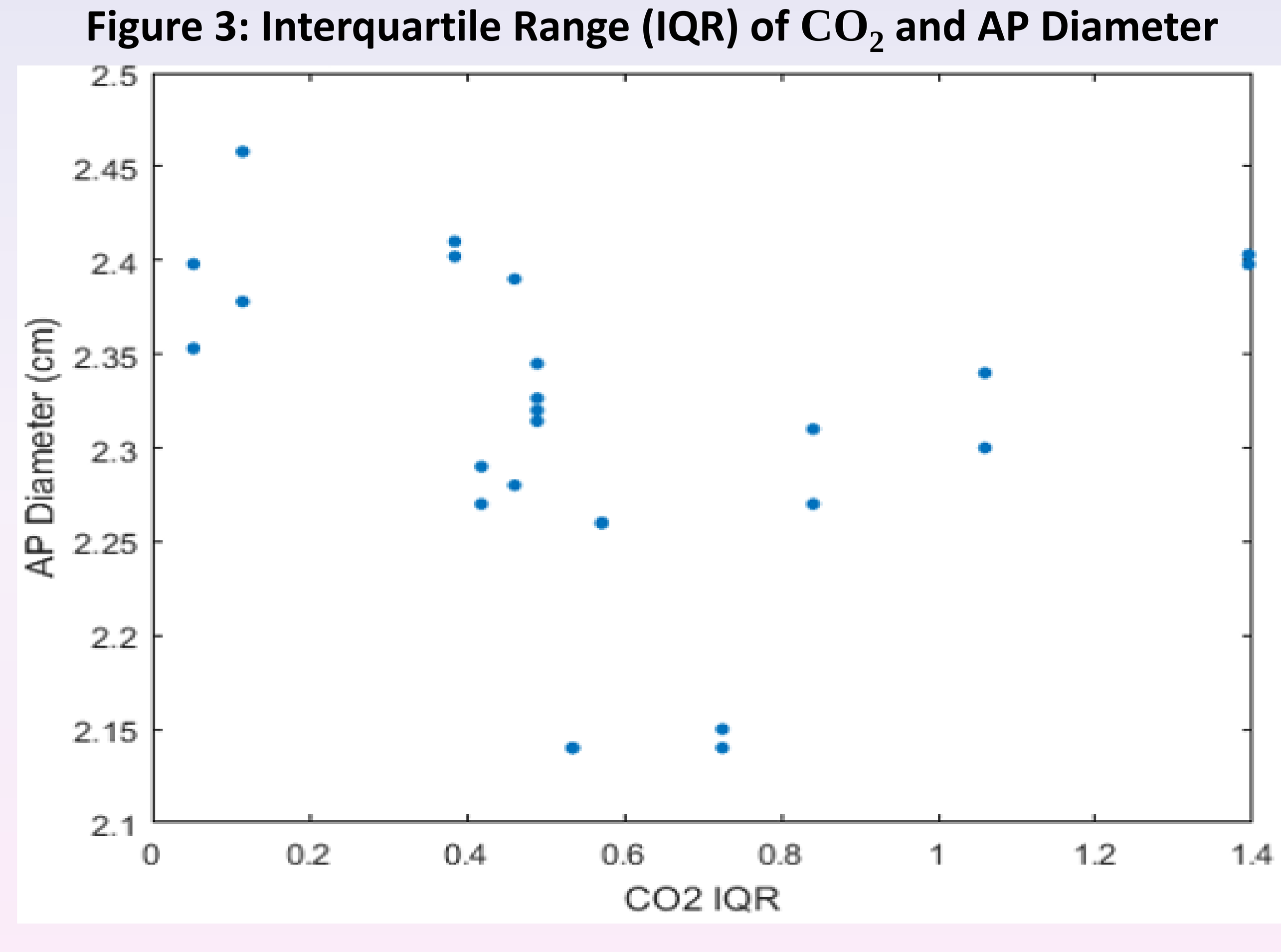


Table 2: Summary of CO2 Readings

	CO2 (mm Hg)
Mean	2.82
Standard Deviation	0.96
Maximum Value	8.50
Minimum Value	0.74
Median Value	2.64
Variance	0.93
Interquartile Range	1.20
Average Terrestrial CO_2	0.3

Figure 3: Interquartile Range (IQR) of CO_2 and AP Diameter

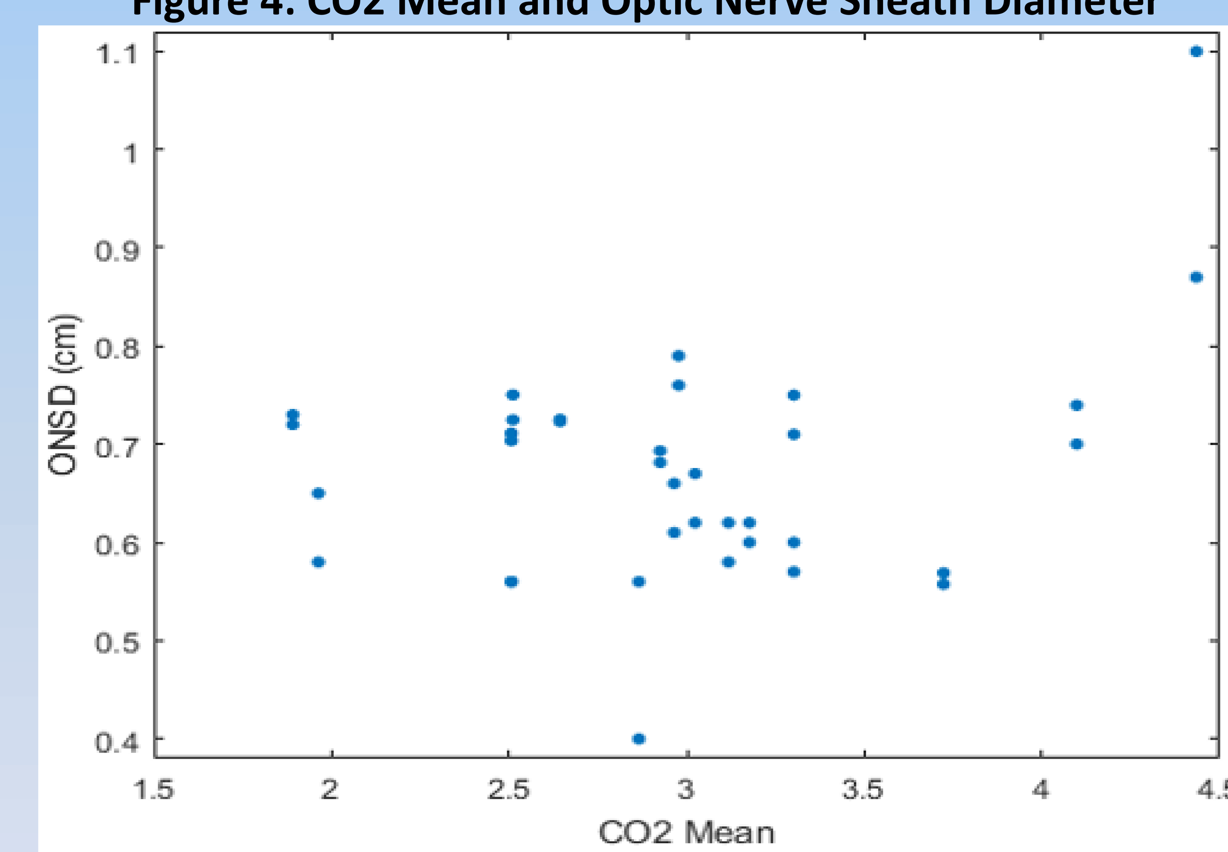


Discussion

This preliminary assessment shows an association between CO_2 variability and AP diameter. There is an association between larger interquartile range and a decrease in AP diameter (Figure 3), suggesting more globe flattening with higher CO_2 variability. Possible mechanism for the reduction in AP diameter includes increased pressure on the back of the eye due to increased ICP or choroidal engorgement. Our analysis also shows that ONSD increases with higher average CO_2. If this association continues to hold when assessing change in AP diameter and ONSD, it may merit a better assessment of the posterior globe. Evaluating choroidal involvement using Optical Coherence Tomography (OCT) data would further elucidate this phenomenon.

In this exploratory analysis, the higher CO_2 mean levels associated with larger ONSD suggests a relationship between CO_2 and increased ICP (Figure 4). However, additional analysis using a more complete dataset is needed to determine whether this relationship truly exists. Comparison to pre-flight ONSD values would be more compelling since there is not a well-established normal range of ONSD in a healthy cohort.

Figure 4: CO2 Mean and Optic Nerve Sheath Diameter



Future work includes filling in the June 2011 – January 2012 gap by adding CO_2 data up to present day, and acquiring readings from additional sensors. Further investigation is needed to explore the relationship between CO_2 and other eye measurements (tortuosity, Doppler hemodynamics, and OCT exams). If the times with CO_2 sensor errors are correlated with any of the outcome measurements, results may be confounded. It may be beneficial to include other CO_2 metrics such as area under the curve (mean CO_2 by time) or only reading CO_2 concentrations within 1 to 2 days of testing. Also, analysis should expand to include preflight eye measurements as a predictor variable to evaluate whether there are actual changes in eye physiology.

Limitations

Because inflight ultrasounds were not conducted on ISS until 2009, only 9 subjects were used in the analysis. Repeated readings of CO_2 levels that lasted more than 20 minutes or values of less than or equal to 0 were removed because this was believed to be a sensor fault or error. Due to the slow download speed, measurements used in the analysis were bounded to readings from 26 March 2009 to 19 October 2012. The limited amount of CO_2 data, along with in-flight ultrasound availability, restricted the number of subjects that could be used in this analysis.