

Within-diver variability in venous gas emboli (VGE) following repeated dives

David J Doolette^{1,2}, F Gregory Murphy¹

¹ Navy Experimental Diving Unit, Panama City, Florida, USA

² Department of Anaesthesiology, University of Auckland, New Zealand

Corresponding author: Associate Professor David J Doolette, Navy Experimental Diving Unit, Panama City, Florida, USA

ORCID: [0000-0001-9027-3536](https://orcid.org/0000-0001-9027-3536)

david.j.doolette.civ@us.navy.mil

Keywords

Bubbles; Decompression sickness; Diving; Echocardiography; Risk

Abstract

(Doolette DJ, Murphy FG. Within-diver variability in venous gas emboli (VGE) following repeated dives. *Diving and Hyperbaric Medicine*. 2023 December 20;53(4):333–339. doi: [10.28920/dhm53.4.333-339](https://doi.org/10.28920/dhm53.4.333-339). PMID: [38091593](https://pubmed.ncbi.nlm.nih.gov/38091593/).)

Introduction: Venous gas emboli (VGE) are widely used as a surrogate endpoint instead of decompression sickness (DCS) in studies of decompression procedures. Peak post-dive VGE grades vary widely following repeated identical dives but little is known about how much of the variability in VGE grades is proportioned between-diver and within-diver.

Methods: A retrospective analysis of 834 man-dives on six dive profiles with post-dive VGE measurements was conducted under controlled laboratory conditions. Among these data, 151 divers did repeated dives on the same profile on two to nine occasions separated by at least one week (total of 693 man-dives). Data were analysed for between- and within-diver variability in peak post-dive VGE grades using mixed-effect models with diver as the random variable and associated intraclass correlation coefficients.

Results: Most divers produced a wide range of VGE grades after repeated dives on the same profile. The intraclass correlation coefficient (repeatability) was 0.33 indicating that 33% of the variability in VGE grades is between-diver variability; correspondingly, 67% of variability in VGE grades is within-diver variability. DCS cases were associated with an individual diver's highest VGE grades and not with their lower VGE grades.

Conclusions: These data demonstrate large within-diver variability in VGE grades following repeated dives on the same dive profile and suggest there is substantial within-diver variability in susceptibility to DCS. Post-dive VGE grades are not useful for evaluating decompression practice for individual divers.

Introduction

Decompression sickness (DCS) is caused by intracorporeal bubble formation from supersaturated dissolved gas. Venous bubbles (venous gas emboli [VGE]) are easily detected by ultrasonic methods and their profusion graded on an ordinal scale. These are widely used as a surrogate endpoint instead of DCS in studies of decompression procedures, both because VGE occur commonly after diving whereas DCS is rare, and because VGE profusion is presumed to be correlated with an increased risk of bubbles forming at or impacting sites where they will cause DCS. Indeed, in large compilations of diving data with both DCS and VGE outcomes, cumulative incidence of DCS increases with increasing peak post-dive VGE grades.^{1,2} However, there is no VGE grade that has both good sensitivity and specificity for DCS and peak post-dive VGE are highly variable following dives on the same dive profile (depth/time/breathing gas history).²

Despite these limitations, there are emerging trends toward interpreting VGE grades measured in an individual diver. Notably, divers can now purchase equipment used for

self-monitoring of post-dive VGE and are using the result to provide feedback on modifying future decompression practice.^{3,4} A future application of VGE measurements could be real-time physiological monitoring during diving for real-time control of decompression.⁵ Validity of these emerging and potential applications of individual VGE measurements relies on an understanding of the within-diver variability in VGE grades as well as the association of VGE grades to DCS in individual divers. However, little is known about how much of the variability in post-dive VGE grades is proportioned between-diver and within-diver.^{6,7}

The current study is a retrospective examination of within-diver variability of VGE grades. The U.S. Navy Experimental Diving Unit (NEDU) has previously published results of several large trials in which several dive profiles were each dived many times under controlled laboratory conditions. In these trials, the same divers often repeated the same dive profile on multiple occasions, separated by at least one week, and VGE were measured after each repeated dive. These data were analysed for within-diver variability in peak post-dive VGE grades.

Methods

The data analysed in this paper were collected during four dive trials approved by the NEDU Institutional Review Board.⁸⁻¹² Informed consent for those trials included consent for de-identified data to be used for future research. Six dive profiles were tested in these four dive trials (see DIVE PROFILES section). Diver-subjects dived these dive profiles one or more times. For the present report, repeated dives are more than one dive by the same diver on the same one of these six dive profiles. Divers refrained from any hyperbaric or hypobaric exposure for two or three days before and after each experimental dive, and in practice, repeated dives were typically at least one week apart. Full details of the dive trials are available in the original reports and only relevant details are summarised here.⁸⁻¹²

All diving occurred in the NEDU Ocean Simulation Facility hyperbaric chamber and wet pot complex. Diving depth was simulated by pressurising the chamber complex with air, and pressure was controlled to approximately 0.5 feet of sea water (fsw, 1 fsw = 3.0643 kPa) accuracy. Chamber atmosphere and wet pot water temperature were actively controlled. Temperatures were sampled at ≥ 0.5 Hz and the means for each dive were computed. Descents and ascents, bottom times, and decompression stop times were followed to within a few seconds of the prescribed dive schedule.

VGE MONITORING

After surfacing from a dive, divers spent 10 minutes adjacent to the chamber before being escorted to a climate-controlled laboratory where they generally remained seated for the remainder of a two-hour observation period. For each VGE

examination, the diver reclined in the left decubitus position while the heart chambers were imaged (apical long-axis four-chamber view) with transthoracic two-dimensional (2-D) echocardiography. Generally, the same ultrasound equipment and imaging mode was used by the same trained cardiovascular technician for all 2-D echocardiographic imaging for each dive profile. With repeated diving, the ultrasound operator and the divers themselves became familiar with the best window for obtaining a 4-chamber apical view in each diver.

Venous gas emboli in the right heart chambers were graded according to one of two ordinals scales shown in Table 1.^{2,13,14} The same scale was used throughout all testing of a dive profile, but to aid comparison between dive profiles for the present analysis, modified Eftedal-Brubakk grades 3 and 4a and grades 4b and 5 were collapsed to single grades approximately equivalent to NEDU grades 3 and 4 respectively. At each examination, VGE were graded three times: after the diver had been at rest on the examination table for approximately one minute and then after three forceful limb flexions around the right elbow and the right knee to elicit a bubble shower. For the movement conditions, the grade assigned was the highest signal sustained for at least four cardiac cycles for grades 1–3 or for about 0.5 s for higher grades. Grades (NEDU scale) were assigned at the time of measurement by the same author (DJD). Modified Eftedal-Brubakk grades were also assigned by either of the present authors, however inter-rater reliability is high for the Eftedal-Brubakk scale,¹³ and the two authors routinely graded ultrasound images together to maintain concordance. For each man-dive, the peak grade of all resting examinations and the peak grade of all resting and limb flexion examinations were analysed; for compactness

Table 1
Venous gas emboli grading scales

Grade	Modified Eftedal-Brubakk	Grade	NEDU
0	No bubbles	0	No bubbles
1	Occasional bubbles	1	Rare (fewer than 1/s) bubbles
2	≥ 1 bubble / 4 heart cycles	2	Several discrete bubbles visible
3	≥ 1 bubble / heart cycle		
4a	≥ 1 bubble / cm ² in all frames	3	Multiple bubbles/cycle, not obscuring image
4b	≥ 3 bubble / cm ² in all frames		
5	Whiteout, individual bubbles cannot be discerned	4	Bubbles dominate image, may blur chamber outlines

these are hereafter denoted as 'resting' or 'movement' VGE grades respectively.

DIVE PROFILES

Two dive profiles were air decompression dives to 170 fsw, 52 metres of seawater (msw) (622 kPa) for 30 minutes bottom time.⁸ Divers were immersed throughout the dives and the mean water temperatures ranged from 29.5°C to 30.8°C. Divers performed approximately 135 W of continuous work on an electrical-hysteresis-braked cycle ergometer during the time at bottom. Divers rested in a seated position during decompression. Examinations for VGE were at around 30 minutes and two hours post-dive. Imaging was undertaken using a Siemens Medical Solutions Acuson Cypress Portable Colorflow Ultrasound System with a 2.5 MHz cardiac probe. The NEDU scale was used for grading VGE. The two dive profiles each had 174 minutes of total decompression stop times but differed in the distribution of time among stop depths. One dive profile had a traditional distribution of stop time and resulted in three DCS cases in 192 man-dives (3/192); 38 divers performed a total of 159 repeated dives on this dive profile. The other dive profile had a 'deep stops' distribution of stop time and resulted in 10 DCS cases in 198 man-dives (10/198); 49 divers performed a total of 172 repeated dives on this dive profile.

Two dive profiles were nitrogen-oxygen dives to 113 fsw (34.4 msw, 448 kPa; 132 fsw [40.2 msw] equivalent air depth) for 155 minutes time at bottom. Divers were at rest and dry throughout the dive and the mean chamber atmosphere temperatures ranged from 20.9°C to 26.7°C. Examinations for VGE were at around 29, 66, and 103 minutes post-dive. The two dive profiles each had 251 minutes of oxygen decompression stops but differed in the total oxygen time and air break time. One dive profile had 30-minute oxygen periods followed by six-minute air breaks and resulted in two DCS cases in 96 man-dives (2/96); 24 divers performed a total of 69 repeated dives on this dive profile. The other dive profile had either 12-minute oxygen periods followed by six-minute air breaks or 24-minute oxygen periods followed by 12-minute air breaks (same totals of oxygen and air break times) and resulted in 8 DCS cases in 136 man-dives (8/136). These slightly different air break schedules had similar probability of DCS and were considered equivalent and treated as one dive profile; 34 divers performed a total of 119 repeated dives on this dive profile. There were some variations in the VGE monitoring during this dive trial. Examinations were made by four different ultrasound operators. For the first 45 man-dives, VGE were detected using the same equipment described in the preceding paragraph after which this machine was replaced with a Sonosite M-Turbo ultrasound with a p21 5-1 MHz cardiac probe and VGE were detected using harmonic imaging. Fourteen divers had VGE measurements from different ultrasound machines on repeated dives. For the first 81 man-dives VGE were graded according to the

original Eftedal and Brubakk scale with the 4a and 4b grades collapsed into a single grade 4. Remaining dives were graded with the modified Eftedal-Brubakk scale. The use of both the original and modified scales had trivial effect on overall within-diver variability: potentially increasing VGE grade variability between repeated dives for five diver-profile groups and decreasing variability for two diver-profile groups.

One dive profile was an air decompression dive to 132 fsw (40.2 msw, 506 kPa) for 20 minutes bottom time with a 9-minute decompression stop at 20 fsw (6.1 msw, 163 kPa).^{11,12} Divers were immersed throughout the dive and the mean water temperatures ranged from 29.8°C to 29.9°C. Divers performed approximately 75 W of continuous work on an electrical-hysteresis-braked cycle ergometer during the time at bottom. Divers rested in a seated position during decompression. Examinations for VGE commenced at approximately 15 minutes after surfacing and continued at 20-minute intervals throughout the two-hour post-dive period. In this study and the one described in the next paragraph, VGE were imaged using a GE LOGIQ e R7 with a 3SC-R7 1.7–4.0 MHz phased array cardiac probe and tissue harmonic imaging. Venous gas emboli were graded using the modified Eftedal-Brubakk scale. This dive profile resulted in no DCS cases in 96 man-dives (0/96); 32 divers performed a total of 71 repeated dives on this dive profile.

One set of dives were 5–8 hour duration, closed-circuit rebreather dives.¹⁰ This was a test of six decompression schedules that were computed with the same decompression algorithm, and this algorithm was designed to produce schedules with the same probability of DCS. Consequently, these six schedules were treated as the same dive profile for the present analysis. Dives ranged from 160 fsw (48.8 msw, 592 kPa) to 200 fsw (60.9 msw, 714 kPa) for bottom times of 82 to 150 minutes. Divers were immersed throughout the bottom time and initial ascent and were breathing 1.3 atm PO₂ helium-oxygen. Divers performed weightlifting and treadmill work during the time at bottom. Decompression stops were in the dry with divers seated at rest and breathing 1.3 atm PO₂ nitrogen-oxygen with air breaks. The mean water temperatures ranged from 27.0°C to 27.5°C and the mean chamber air temperatures ranged from 24.0°C to 25.4°C. Examinations for VGE commenced 20 minutes after surfacing and continued at 30-minute intervals throughout the two-hour post dive period. Venous gas emboli were graded using the modified Eftedal-Brubakk scale. These dives resulted in one DCS case in 120 man-dives (1/120); 28 divers performed a total of 103 repeated dives on these schedules.

VGE VARIABILITY ASSESSMENT

In total, 244 divers performed the 838 man-dives resulting in 24 DCS cases. All these data were used to rank the profiles according to cumulative incidence of DCS. Venous gas

emboli grades were not available for four man-dives: two cases of DCS and one other medical incident onset before VGE measurements, and VGE grades were lost for one man-dive. The remaining 834 dives will be referred to as the pooled data. In the pooled data there were 141 single dives (i.e., divers only performed one dive on a dive profile) and there were 151 divers who performed 202 groups of repeated dives (total of 693 repeated man-dives). There are fewer divers than diver-profile groups because some divers performed repeated dives on two dive profiles and are therefore represented by two diver-profile groups.

Ordinal logistic mixed-effect models of the form:

$$\log \left(\frac{P(y_{ij} \leq k)}{P(y_{ij} > k)} \right) = \beta_0 + \beta_1 x + \alpha_i + \varepsilon_{ij} \tag{Equation 1}$$

were fit to the VGE grades in the pooled data where y_{ij} is the VGE grade for the i^{th} individual on the j^{th} occasion, $k = 0, 1, 2, 3$, β_0 and β_1 are the fixed effects (population intercept and dive profile), x indicates the dive profile, α_i is the random effect (diver) assumed to have a normal distribution with a mean of zero and variance σ_α^2 , and ε_{ij} is a random error assumed to have the standard logistic distribution with a mean of zero and a variance $\sigma_\varepsilon^2 = \pi^2/3$.¹⁵ Variability in VGE grades between diver-profile groups was assessed using the intraclass correlation coefficient calculated from the residual variances of the models as:¹⁵

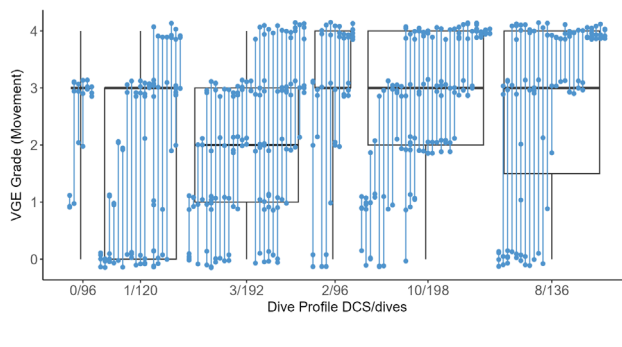
$$\frac{\sigma_\alpha^2}{\sigma_\alpha^2 + \sigma_\varepsilon^2} \tag{Equation 2}$$

where σ_α^2 were the group variances taken from the model output. Variability in VGE grades within diver-profile groups was one minus the intraclass correlation coefficient. Models were fit to the VGE grades using the ordinal package (v 2019.12-10, Christensen, RHB. Ordinal – regression models for ordinal data. 2022. URL: <https://CRAN.R-project.org/package=ordinal>) in R (v 4.2.2. R Core Team. R: A language and environment for statistical computing. Vienna, Austria R: Foundation for Statistical Computing; 2022. URL: <https://www.R-project.org/>).

Two analyses were performed to assess the impact of treating equivalent decompression schedules as the same in two of the dive profiles. The intraclass correlation coefficient was calculated for a variant of the pooled data, in which the two equivalent air break schedules in the 8/136 dive profile were separated. This approach was unsuitable for the 1/120 dive profile because there were relatively few repeated dives in each of the six equivalent schedules; instead, the intraclass correlation coefficient was calculated for a subset of the pooled data that excluded the 1/120 dive profile.

Figure 1

Venous gas emboli (VGE) grades for the six dive profiles; Y-axis is peak post-dive movement VGE grade. Dive profiles are identified on the x-axis by the number of DCS and number of all man-dives as given in the methods. Box and whisker plots show the median, interquartile range, and range of VGE grades for the pooled data ($n = 834$). The corresponding subsets of three or more repeated dives ($n = 517$) are illustrated with blue points and lines. Blue points are VGE grades for individual man-dives. Points are jittered vertically (random shift of up to ± 0.15 grade) to reduce overlap of points of the same grade. Blue lines connect VGE grades for repeated dives by the same diver



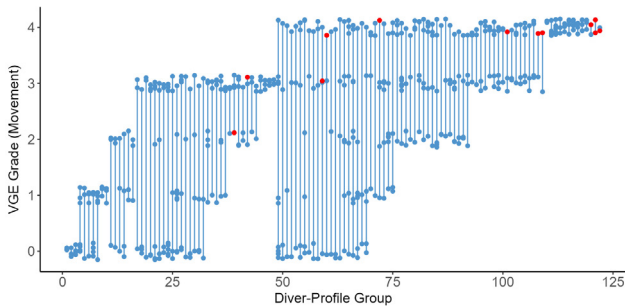
Results

Figure 1 shows the movement VGE grades for the six dive profiles. The dive profiles are shown from left to right in increasing order of DCS cumulative incidence for all man-dives (pooled data plus the four missing VGE grades). The box and whisker plots show the median, interquartile range, and range of VGE grades for the pooled data. Although there is large variability in peak VGE grades following the same dive profile, there is a general shift of interquartile range to higher grades with increasing DCS cumulative incidence. Vertical blue lines connect groups of VGE grades for repeated dives by the same diver and the blue points illustrate the individual movement VGE grades for a subset of three or more repeated dives (single dives and two repeated dives are excluded to reduce clutter). Post-dive VGE for repeated dives by the same diver are highly variable.

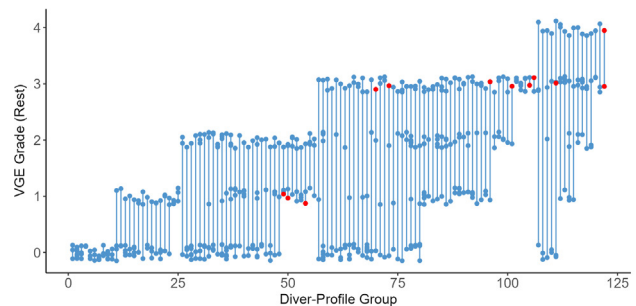
Figure 2 shows individual movement VGE grades for a similar subset of dives as in Figure 1. In addition to three or more repeated dives, Figure 2 includes the five diver-profile groups of two repeated dives in which DCS occurred. In Figure 2, diver-profile groups of repeated dives are ordered by maximum then minimum VGE grade within the group, irrespective of the dive profile. This ordering clusters together diver-profile groups of similar variability. In this subset, 21 divers (22% of divers, 17% of diver-profile groups) had the same VGE grade after repeated dives. Of these consistent bubblebers, the majority are divers who routinely produced grade 4 VGE, and this may be partly a ceiling effect since this is the highest discernable grade.

Figure 2

Movement VGE grades and DCS for three or more repeated dives and the five diver-profile groups of two repeated dives in which DCS occurred ($n = 527$). The Y-axis is peak post-dive movement VGE grade. Points are VGE grades for individual man-dives (points are jittered vertically – random shift of up to ± 0.15 grade to reduce overlap of points of the same grade). Blue points are VGE grades for dives that did not result in DCS; red points are VGE grades for dives that resulted in DCS. Blue lines connect VGE grades for repeated dives. The 122 diver-profile groups are ordered along the x-axis by increasing VGE grades

**Figure 3**

Resting VGE grades and DCS for three or more repeated dives and the five diver-profile groups of two repeated dives in which DCS occurred ($n = 527$). The Y-axis is peak post-dive resting VGE grade. Points are VGE grades for individual man-dives (points are jittered vertically – a random shift of up to ± 0.15 grade to reduce overlap of points of the same grade). Blue points are VGE grades for dives that did not result in DCS; red points are VGE grades for dives that resulted in DCS. Blue lines connect VGE grades for repeated dives. The 122 diver-profile groups are ordered along the x-axis by increasing VGE grades



There were fewer consistent bubblers (2–4 divers) at any of the lower movement VGE grades. Figure 3 shows the resting VGE grades for the same subset of repeated dives as in Figure 2; there are few consistent bubblers, but the majority of these are divers who routinely produced no resting VGE.

For movement VGE grades in the pooled data set, intraclass correlation calculated from the ordinal logistic model was 0.33. The pooled intraclass correlation indicates that 33% of the variability in VGE grades is between-diver variability; correspondingly, 67% of variability in VGE grades is within-diver variability. For the resting VGE grades in the pooled data set, intraclass correlation for the grades was 0.37. For movement VGE grades in the pooled data, separating the two equivalent air break schedules in the 8/136 dive profile or leaving them combined resulted in no difference in intraclass correlation coefficient (0.33 in both cases). For movement VGE grades in the subset of the pooled data excluding the 1/120 dive profile, the intraclass correlation coefficient was 0.30, slightly lower than for the pooled data set. These results indicate that combining the equivalent schedules into single dive profiles did not increase within-diver variability in VGE grades in the pooled data.

Figure 2 shows the movement VGE grade in red for those repeated dives that resulted in DCS. There are only 12 cases DCS in this subset of repeated dives; nevertheless, it is striking that DCS was not confined to divers who routinely produce high bubble grades. Instead, DCS mostly occurred in divers with variability in VGE grades, but occurred in association with diver's highest or second highest VGE grade. Eleven of these DCS cases manifested as joint pain in the knees or shoulders. One diver had pruritic, mottled skin rash in association with grade 4 VGE after both repeated dives. Figure 3 shows three of the 12 DCS

cases are associated with a diver's lowest peak post-dive resting VGE grade after repeated dives. This apparently degraded association of DCS cases with resting VGE grade compared with movement VGE grade is interesting but is not significant (χ^2 test of proportions of DCS cases associated with maximum VGE grade, $P = 0.816$).

Discussion

The large variability in pooled peak VGE grades following identical dive profiles has been previously reported.^{2,16} However, the present study is the first to show that this variability is principally due to within-diver variability in VGE grades. This within-diver variability in VGE grades is not attributable to differences in monitoring techniques because measurements were typically done with the same equipment, by the same ultrasound operator, and graded by the same investigator. The high within-diver variability in VGE grades occurs despite no practical variation in the diving and post-dive VGE monitoring period (dive profile, work, thermal status). Therefore, this variability in VGE grades must be caused by variability in some intrinsic host factor or pre-dive environmental factor that was not, or possibly cannot be, controlled.

The correlation of cumulative incidence of DCS with peak VGE grades has previously been reported for pooled data.^{1,2} The present study is the first to indicate that DCS is associated with an individual diver's highest VGE grades and not with their lower VGE grades after repeated dives. It is noteworthy that most DCS were joint pain. Whereas some manifestations of DCS are thought to result from VGE or right-left shunt of VGE, DCS joint pain is thought to result from bubbles in the tissues.^{17,18} The association of DCS joint pain with a diver's VGE grades suggests an individual diver's

risk of DCS, irrespective of the pathophysiology, varies with VGE grades. The large variability in peak VGE grades after repeated dives might be interpreted as evidence of substantial day-to-day (within-diver) variability in DCS susceptibility.

The most obvious implication of the present findings is that monitoring of VGE following uncontrolled field dives is not useful for evaluating and recommending decompression practice for individual divers. Since an individual diver manifests widely varying peak VGE grades following carefully controlled repeated dives that are identical for all practical purposes, different VGE grades following successive uncontrolled field dives cannot be attributed to differences in decompression practice. The present findings do suggest that an individual diver's greatest risk of DCS coincides with high post-dive VGE grade, but this information has limited operational application. Post-dive intervention to mitigate the risk of DCS (such as surface oxygen breathing or recompression) implemented because of high VGE grade would usually be wasted because even the highest VGE grade has low positive predictive value for DCS (5–13%).^{1,2} Moreover, by the time peak post-dive VGE occur it may often be too late to intervene to prevent DCS: about half of DCS cases onset by the time VGE grades typically peak following long bounce dives.^{19–21}

On the other hand, the apparent association of risk of DCS with an individual's post-dive VGE grades is promising for individualized control of decompression, because it suggests VGE detected *during* decompression may also be usefully associated with risk of DCS. Early laboratory chamber experiments with animals show VGE can be detected during decompression, and VGE numbers altered by changing the decompression profile.²² These observations suggest VGE could be a target for real-time control during decompression if VGE detected during decompression could be shown to be reliably associated with risk of DCS. However, practical methods for evaluating VGE in real-time during actual diving are yet to be developed.

When designing and analysing experimental decompression trials using DCS as the endpoint we have previously interpreted our own observation of within-diver variability in DCS outcomes after repeated dives, along with similar observations during altitude exposures,²³ as evidence of day-to-day (within-subject) variability in DCS susceptibility.^{10,11} We have used this evidence to justify relaxing the typical definition of statistical independence and considered the experimental unit as the man-dive and not the subject. This is expedient because it is impractical to conduct hundreds of man-dives without repeated use of the same volunteers. The large within-diver variability in peak VGE grades and the possible association with variability in DCS susceptibility further supports the use of the man-dive as the experimental unit in studies with DCS as the endpoint. There are similar implications for studies that use peak VGE grade as the primary endpoint. Such studies are frequently designed as

paired comparison of subjects¹⁶ and the large within-diver variability in VGE grade suggest that this design is not necessarily better than an unpaired design for interventions to the dive profile, work, and thermal status.

The present data have the limitation of being assembled from dive trials not designed for the present retrospective analysis. As identified in the methods, for some dive profiles VGE examinations were less frequent than current recommendations.^{14,19} Also, the number of DCS cases after repeated dives was small so must be interpreted cautiously. However, a principal strength is analysis of a VGE data set of a size that is unlikely to ever be produced for a prospective study of variability in VGE grades.

Conclusions

These data demonstrate large within-diver variability in peak VGE grades following repeated dives on the same dive profile and suggest there is substantial within-diver variability in susceptibility to DCS. The well-known association of DCS with VGE grade in pooled data, and the low positive predictive value of that association, are apparent in individual divers. Post-dive VGE grades are not useful for evaluating decompression practice for individual divers.

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