Comparison of three different ultrasonic methods for quantification of intravascular gas bubbles

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Brubakk AO, Aftedal O. Comparison of three different ultrasonic methods for quantification of intravascular gas bubbles. Undersea Hyper Med 2001; 28(3):131–136.—For evaluating different decompression schedules, the use of ultrasound is common. Systems based on the Doppler principle have mostly been used. However, ultrasonic scanners producing images where the bubbles are easily detected, may be an alternative, because analysis of the signals is simpler than when using Doppler methods. In this study, three methods of bubble detection were used following a series of air dives. The divers were investigated using a "blind" Doppler system where only auditory signals were used for positioning the probe. They were also studied using ultrasonic images and finally an "image-assisted" Doppler method was used, where the sample volume of the Doppler system was positioned using the images. Both Doppler systems were pulsed Doppler systems. The agreement between the methods was determined using weighted kappa statistics. The results show that, at rest, the agreement between the images and the blind Doppler method was very good, and between the two Doppler methods and the images and the image-assisted method the agreement was good. Generally, the agreement is better at higher bubble grades. After movement, the agreement was not good. We conclude that grades from the different methods can be directly compared at rest.

Doppler, ultrasonic scanning, bubble detection

Ultrasonic Doppler systems have been used extensively for the detection of gas bubbles in the pulmonary artery (1–3). Gas bubbles can be heard as high intensity chirps in the blood flow signal and the signals are graded according to a grading system (4,5).

Doppler grading systems can be used to distinguish between safe and unsafe profiles. Generally, the Doppler methods show a relationship between the bubble grade and the incidence of decompression illness (DCI) (6–8), with the risk of clinical symptoms increasing significantly if high bubble grades are seen. However, the overall correlation between Doppler scores and the incidence of DCI is inconsistent (9). Sawatzky (10) showed that at least one single observation of grade III bubbles was detected in 95% of all divers with clinical symptoms of DCI. However, a considerable number of individuals with grade III bubbles do not exhibit any clinical signs of DCI.

The use of an ultrasonic scanning technique has been introduced for evaluating gas bubbles in the pulmonary artery. It has been shown that inexperienced observers, using a dedicated grading system, were able to grade the bubbles in images as accurately as well-trained observers could grade Doppler data (11), but a comparison of image and Doppler grading has previously not been performed. In this study we compare the image grading system with the established grading system described by Spencer (2).

MATERIAL AND METHODS

Ultrasonic measurements were performed after experimental air dives using surface decompression. Decompression was performed using a standard U.S. Navy surface decompression table and an experimental table based on the concept of bubble growth index (BGI) (12;13).

The images were obtained using a Vingmed 750 ultrasonic scanner (Vingmed Sound a/s, Vingmed, Horten, Norway), connected to an ultrasonic transducer using a frequency of 3.5 MHz. The investigation was performed with the diver lying on his left side, using a parasternal longitudinal view of the right ventricle and the pulmonary artery. Bubbles can be detected as white spots. The number of bubbles was scored according to the grading system given below (Table 1).

To obtain Doppler signals, the transducer position was maintained, and the sample volume of the pulsed mode system was positioned inside the pulmonary artery by watching the images. Care was taken to place the sample volume in a position where signals from walls and the pulmonary valve could not be heard. In Results, this method is described as the "image-assisted" Doppler method. Bubbles can be heard as chirps in the audio signal and were scored using the Spencer grading system, as described below

The "blind" Doppler measurements were performed

Table 1: Grading of Ultrasonic Images

Grade	Description
0	no bubbles
1	occasional bubbles
2	at least one bubble/4th cycle
3	at least one bubble every cycle
4	continuous bubbling, at least one bubble · cm^2
5	"White-out", individual bubbles cannot be seen (this grade has been observed only in animals and is not used in this study)

using a pulsed Doppler ultrasonic system with a 2-Mhz transducer (Alfred, Vingmed Sound a/s) This system measures the velocities inside a cylindrical sample volume of approximately 2 cm in diameter and 7.5 mm length. The probe was positioned on the left sternal border in the second or third intercostal space. The diver was resting on the left side. The position of the sample volume was determined by listening to the Doppler shift, a position giving a good flow signal with as little valve noise as possible was used. In Results, this method is described as the blind Doppler method.

Ninety-two measurements were performed using both the blind and the image-assisted Doppler method. The sequence of the measurements were random and performed by two different observers, who were not aware of the result of the other investigation.

A total of 340 measurements were performed, where images and image-assisted Doppler data were obtained. The image data were always obtained before the Doppler data; the same individual performed the scoring for both methods.

All data above were obtained with the divers at rest. In addition, the two Doppler methods were used in 31 measurements immediately after the divers had performed three deep knee bends. Furthermore, a comparison between the image and image-assisted Doppler method was performed in 28 divers after the same exercise. All data were evaluated in real time.

Evaluation of ultrasonic grades: The ultrasonic images were evaluated using a grading system with a scale from 0 to 4 (11) (Table 1). The Kisman–Masurel (K–M) grading system was used for evaluating the blind Doppler (4). This scale was converted into the Spencer scale using the conversion table given by Nishi (7). The image-assisted Doppler signals were evaluated partly using the Spencer grading system (2) and partly the K–M system. The reason was that not all observers were properly trained in using the K–M system. The K–M grading system gives a more detailed classification but the results can easily be converted to the Spencer grade (7).

The ultrasonic images were evaluated using a grading system with a scale from 0-4 (11) (Table 1). If large volumes of gas were observed, typically grade 4 and in some cases grade 3, the data were transferred to a computer for counting of the bubbles (13). This program identifies all signals with an intensity above a certain threshold in the blood stream and counts these signals in each image. The results of this study will be published elsewhere.

Statistics: We used the weighted kappa statistics to look at the agreement between the different grading methods. This statistical method is designed for ranked or nominal data and gives a coefficient of agreement, κ_w, in the range from −1.0 to +1.0, where +1.0 represents perfect agreement, 0.0 represents agreement equal to chance, and the negative values represent less agreement than would be expected by chance. Deviations are weighted, i.e., small disagreements are believed to be more corrected than large disagreements, and the method is completely corrected for chance agreement. This weighing gives 100% credit for complete agreement, 75% credit for one category disagreement, and so on, down to 0% credit for five categories of disagreement. Details of the method area given by Altman (14). The values are given ± SE.

The evaluation of the κ_w statistics, giving the strength of agreement, can be seen in Table 2.

RESULTS

Resting divers: In Table 3, a comparison of the "blind" Doppler method with the image-assisted Doppler method is shown.

Of the 92 observations, 62 (67%) were identical. In the rest, nearly all of the blind Doppler measurements were given a bubble grade higher than the image-assisted ones. This is particularly true for those graded II in the image-assisted system, where 11 out of 14 had grade III on the "blind" system. Eight of those 11 had grade 3 in the images.

A total of 340 measurements were performed where the image-assisted Doppler score was recorded together with the image scores. The results can be seen in Table 4. In 205 cases (57 %) there was a total match between

Table 2: Evaluation of Weighted Kappa Statistics

Agreement	κ_w value
Poor	< 0.20
Fair	0.21–0.40
Moderate	0.41–0.60
Good	0.61–0.80
Very good	0.81–1.00

Table 3: Comparison at Rest

Blind Doppler → / Image Doppler ↓		0	I	II	III	IV	Total
	0	**41**	5	2	0	0	48
	I	0	**14**	8	2	0	24
	II	0	0	**3**	11	0	14
	III	0	0	2	**4**	0	6
	IV	0	0	0	0	**0**	0
Total count		41	19	15	17	0	92

the two scores, in the rest of the cases, the image score was above the image-assisted Doppler score. This is particularly the case for grade 3 in the images, where 69% of the observations had an image-assisted Doppler score of II.

A comparison was also made between the images and the blind Doppler, the results can be seen from Table 5. There was total agreement between the two methods in 82% of the cases.

The three methods were also compared after the diver had performed three knee bends. The results can be seen from the three tables below (Tables 6–8). The agreement between the methods is not as good as it is at rest. There is a tendency to give higher bubble grades when blind Doppler is used (Tables 6 and 8). This can probably be explained by an increased movement of valves and walls that could be mistaken for bubble sounds.

When images are compared to blind Doppler, agreement between the two methods was only seen in 39% of the cases, in the majority of the other cases, the blind Doppler gave higher grades.

Table 9 shows the κ_w statistics for the different methods. From this we can see that the best agreement is between blind Doppler and images (very good). Both the other comparisons showed good agreement at rest, while the agreement was less good after movement. This could be caused by more movement of valves and walls following exercise, but also because an increase in the number of bubbles only lasts for a short period of time and the measurements were not performed simultaneously.

DISCUSSION

The study presented here shows that, at rest, there is a good agreement between the different methods of grading ultrasonic data (Table 9). However, there also are some important differences between the methods for analyzing ultrasonic data. Several factors may influence our results.

The sensitivity of the ultrasonic equipment for detecting bubbles is difficult to determine. The detection of gas bubbles using ultrasound is dependent on the fact that gas is a good reflector for ultrasound. Above resonant frequency, there is a linear relationship between the intensity of the reflected signal and the cross sectional area of the gas bubble (15).

At the surface, the resonant bubble size for the ultrasonic frequencies used here is between 1.5 and 1 μm (16). This is the size indicated for bubble nuclei (17), thus it is not unreasonable to believe that gas bubbles in the blood will have a size considerably above that. Daniels and colleagues (18) demonstrated experimentally that the lowest bubble size detectable with ultrasound was of the order of 10 μm. In man, using external transducers, the minimum detectable size is probably substantially above this.

However, as all three methods are dependent on the same principle of detection, there is no reason to believe that there is a significant difference in sensitivity of the three methods, in spite of differences in equipment, frequencies, and detection method. The threshold for detection of single bubbles will decrease with increasing frequencies and with an increase in transducer size (19), thus giving the image-based system a slight advantage. On the other hand, the lower ultrasonic frequencies are less attenuated, giving a slight advantage to the blind Doppler system. The signal-to-noise ratio for the blind Doppler method is probably lower than for the two others, as signals from valves and vessel walls may add to the noise. In our experience, when few bubbles are present it is mostly easier to detect them visually if the image quality is good. In some individuals, the image quality is less good and the bubbles are then easier heard

Table 4: Comparison at Rest

Images → / Image Doppler ↓		0	1	2	3	4	Total
	0	**103**	31	2	0	0	136
	I	3	**47**	34	3	0	87
	II	0	0	**24**	53	0	77
	III	0	0	0	**30**	9	39
	IV	0	0	0	0	**1**	1
Total count		106	78	60	88	8	340

Table 5: Comparison at Rest

Images →	0	1	2	3	4	
Blind Doppler ↓						Total
0	**39**	1	0	0	0	40
I	2	**15**	1	0	0	18
II	0	4	**9**	1	2	16
III	0	1	4	**12**	0	17
IV	0	0	0	0	**0**	0
Total count	41	21	14	13	2	91

Table 6: Comparison After Movement

Blind Doppler →	0	I	II	III	IV	
Image Doppler ↓						Total
0	**2**	3	2	1	0	8
I	0	**0**	0	5	1	6
II	0	0	**2**	4	4	10
III	0	0	2	**3**	2	7
IV	0	0	0	0	**0**	0
Total count	2	3	6	13	7	31

Table 7: Comparison After Movement

Images →	0	1	2	3	4	
Image Doppler ↓						Total
0	**6**	1	0	2	0	9
I	0	**1**	0	5	0	6
II	0	0	**0**	10	0	10
III	0	0	0	**4**	2	6
IV	0	0	0	0	**0**	0
Total count	6	2	0	21	2	31

Table 8: Comparison After Movement

Images →	0	1	2	3	4	
Blind Doppler ↓						Total
0	**3**	0	0	1	0	4
I	2	**0**	0	0	0	2
II	1	1	**0**	1	2	5
III	0	1	0	**11**	0	12
IV	0	0	0	8	**0**	8
Total Count	6	2	0	21	2	31

than seen.

All three methods are based on a subjective evaluation of either the audio signal or the images. Thus possible differences in competence and experience in evaluating the data has to be considered. The images and the image-assisted Doppler were evaluated by the authors, who both have extensive experience. The blind Doppler signals were evaluated by the authors and several investigators, all of them had been trained in evaluating Doppler signals. However, as it has been shown that grading Doppler signals is difficult (20) and requires constant practice, we expected these results would have the greatest uncertainties. The results indicate that this was not the case, as the relationship between blind Doppler and images was very good.

We have previously shown (11) that it is easier to

Tables 9: Strength of Agreement, κ_w Statistics

Comparison	At Rest (±SE)	After Movement (±SE)
Blind Doppler—image-assisted Doppler	0.68 (0.07)	0.19 (0.08)
Blind Doppler—images	0.83 (0.08)	0.45 (0.08)
Image-assisted Doppler—images	0.69 (0.04)	0.41 (0.10)

Table 10: Grading System for Ultrasonic Signals

Grade	Doppler: Spencer Scale	Images: Eftedal/Brubakk Scale
0	a complete lack of bubble signals	no bubbles
I / 1	occasional bubble signal with the cardiac motion signal, the great majority of cardiac periods free of bubbles	occasional bubbles
II / 2	many but less than half of the cardiac periods contain bubble signals, singly or in groups	at least one bubble/4th cycle
III / 3	most of the cardiac periods contain showers of single bubble signals, not dominating the cardiac motion signals	at least one bubble/cycle
IV / 4	maximum detectable bubble signal continuously throughout systole and diastole of every cardiac period, overriding the amplitude of the normal cardiac signal	continuous bubbling, at least one bubble · cm^{-2}

grade images than Doppler signals. This is particularly the case when few bubbles are present. From Table 4 we see that the image-assisted Doppler method detects bubbles only in 60% of the cases where the images are classified as grade 1. For image grades 2 and 3, however, there is better agreement, but the Doppler grades tend to be one grade below the image grade. The image grade 2 covers image-assisted Doppler grades I and II and image grade 3 image-assisted Doppler grades II and III. It is important to keep in mind that the measurements are not performed simultaneously, thus changes in actual bubble numbers between measurements may have influenced the results.

From Table 5 we see that the agreement between images and blind Doppler is generally better, but there is a tendency for the Doppler grades to now seem higher than the image grades. The reason for this may be seen from the results presented in Table 3. The comparison between image-assisted and blind Doppler systems shows that, generally, the blind system gives somewhat higher grades than the image-assisted system. This is not surprising, as signals from valves can give strong signals that can be confused as bubbles. This explanation is supported by the observation that after movement there is an even greater tendency for the blind Doppler to give higher scores (Table 6). Positioning the image Doppler sample volume is easy as you can see exactly where the vessel walls and valves are located and these structures can then be avoided.

These comparisons were made using pulsed ultrasonic systems. Generally in diving research continuous wave systems have been used. These systems have no depth resolution (21) and thus the signal-to-noise ratio will be lower. This may be of importance, particularly if few bubbles are present. As movement from all structures inside the ultrasonic beam will be recorded, this will certainly lower the signal-to-noise ratio and thus increase the risk of falsely recording wall and valve movements as bubble signals.

There is no accepted "gold" standard for bubble counting. However, as is argued above, at least for inexperienced investigators, the imaging system is probably the system closest to this, as bubbles are easy to detect and may be easily graded even by untrained observers (11). Based on this, our results indicate that a blind Doppler system will tend to overestimate the amount of gas present for low bubble grades, but there is good agreement with the image system at higher bubble grades 2 and 3.

The grading systems used in this study are non-linear with respect to the actual number of bubbles present. Based on the data from our animal experiments, we have tried to relate the bubble grade to the number of bubbles in the pulmonary artery (22). This is an approximation, but its main purpose is to demonstrate that the grading system is highly non-linear. According to this, an individual with grade 3 bubbles may have 40 times the number of bubbles than an individual with grade 2. Comparison of different tables is thus difficult using the grading system, due to this non-linearity. Nishi et al. (23) have tried to overcome this by introducing an index of severity that takes this into account. By introducing a conversion to actual bubble numbers, it should be possible to evaluate tables using the number of bubbles.

The number of bubbles may be integrated over time, giving an indication of the total gas stress on the pulmonary artery and the lungs.

In conclusion, this study has shown that there is close correlation between the different methods of grading ultrasonic bubble data. The results indicate that it may be possible to directly compare Doppler and image grades as is shown in Table 10.

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