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LETTERS

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Effect of the probe frequency on sensitivity of color Doppler ultrasound to color blood flow: comment on the article by Torp-Pedersen et al

To the Editor:

I read with great interest the report by Torp-Pedersen et al on the impact of power and color Doppler settings for inflammatory flow on scoring of disease activity in patients with rheumatoid arthritis (1). I agree with the authors' comments on the differences in color Doppler sensitivity to blood flow among different machines, Doppler modalities, and ultrasound settings, and their findings provide good data support for evaluation of the sensitivity of different ultrasound apparati. However, the study conclusion is still a debatable issue, because some important influencing factors may have been overlooked.

In Torp-Pedersen and colleagues' study, 6 types of ultrasound machine with different frequency probes were used. Thus, an important factor should be considered, i.e., the effect of differences in frequency probe on blood flow display. In fact, higher-frequency transducers improve sensitivity to low blood flow (2–4). For clinical Doppler sonography, Rayleigh-Tyndall scattering governs the intensity of the backscattered echoes. If the Doppler frequency doubles (for example from 2 MHz to 4 MHz), signal intensity increases 16-fold (4,5). The greater number of signal results makes higher-frequency transducers more sensitive in scanning superficial flow. On the other hand, high-frequency transducers can yield greater frequency shifts, which obviously increase sensitivity to low flow. Because power Doppler has a better signal-to-noise ratio, its most important benefit is improved flow sensitivity. Power Doppler is most useful in clinical musculoskeletal ultrasound, where optimal sensitivity is required, or when a more robust flow image is desired. With specific reference to rheumatology, use of a higher-frequency probe with power Doppler usually results in increased Doppler signals from the joints of patients with inflammatory arthritis.

Indeed, my colleagues and I have also noticed that color Doppler may appear more sensitive than power Doppler in detecting low blood signals. Nevertheless, Torp-Pedersen and colleagues' statement that "It is a misconception that power Doppler is inherently more sensitive than color Doppler" cannot be confirmed from their reported results. In the study they describe, the differences in sensitivity resulted from the use of different frequency probes. Another important factor may have been the manufacturing quality of the different machines; the use of advanced technology in the manufacture of clinical color Doppler systems is needed in order for them to perform at an excellent level.

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Reply

To the Editor:

We thank Dr. Zhu for his interest in our report and would like to respond to several of the points he raises.

We do not entirely agree with the statement that our findings provide good data support for evaluation of the color sensitivity of different ultrasound apparati. The study was designed to compare color and power Doppler sensitivity within 6 machines, not to make comparisons between the 6 machines. Within each machine, color and power Doppler were used with factory settings and study settings (the latter being our adjustments to increase sensitivity). We did not conclude that one machine was more sensitive than another.

Dr. Zhu contends that higher-frequency transducers improve sensitivity to low blood flow and that if the Doppler frequency doubles (e.g., from 2 MHz to 4 MHz), signal intensity increases 16 times. This refers to the fact that the intensity of the scattered wave (Rayleigh-Tyndall scattering) increases with the fourth power of frequency (1). However, the author of that report also points out "Of course, attenuation in soft tissue also rises with frequency, tending to offset the advantage of the increased efficiency of scattering at higher frequencies" (1). It is therefore difficult to predict which Doppler frequency will provide the optimal performance. This was exemplified in a study in which we compared the sensitivity of Acuson Sequoia 128 and GE Logiq L9 apparati in detecting flow in patients with Achilles tendinitis (2). The 2 machines behaved exactly oppositely when the Doppler frequency was varied within the available spectrum. With the Acuson Sequoia 128, lower frequencies yielded higher sensitivity, and with the GE Logiq L9, higher frequencies yielded higher sensitivity.

Next, Dr. Zhu states that the signal-to-noise ratio obtained with power Doppler is superior to that obtained with color Doppler, making the former more sensitive to flow, and that with specific reference to rheumatology, use of a higher-frequency probe with power Doppler usually results in increased Doppler signals from the joints of patients with inflammatory arthritis. When power Doppler emerged, it seemed to be more sensitive than color Doppler on those machines. Authors describing the technique explained this based on the theoretically better signal-to-noise ratio, and it

has since become taken as "truth" since nearly all authors repeat these statements. It has gone nearly unnoticed in the medical community that in various machines, color Doppler is more sensitive than power Doppler; in the Acuson Sequoia 128 and the GE Logiq L9, for example, this has been the case since 1999 and 2003, respectively.

Rubin and Bude and their group were actually more cautious in their statements than were subsequent authors who cited them, for example, "Although we believe (and our initial experience suggests) that power Doppler sonography is superior to color Doppler sonography in many organs of the body, each organ presents its own special set of scanning circumstances, and it is extremely unlikely that power Doppler sonography will prove superior to color Doppler sonography for all organs under all circumstances" (3) and "Low flow settings in CD [color Doppler] typically use very low pulse repetition frequencies, often resulting in aliasing artifact, which obscures directional information. In this setting, CD is usually performed only to evaluate whether flow is present and/or to provide position information to guide placement of a Doppler sample gate, and, so far, PD [power Doppler] appears to function at least as well as CD in this regard" (4). Thus, when color Doppler is most sensitive (low flow settings), power Doppler appears to be just as sensitive (not better!).

In our study we found that whether color or power Doppler was more sensitive was machine dependent. We did not look into the literature for an explanation—the literature is full of statements that power Doppler is more sensitive due to the better signal-to-noise ratio. Instead, we sought the information from sources where in-depth knowledge of Doppler is present, i.e., in the companies producing the equipment. We received virtually identical responses from 3 companies, saying that detection of a Doppler shift is the same with the 2 modalities. It is the display that is different (as elaborated upon in our report). The following explanation is provided by one of the authors of the present correspondence (JAJ), who is an academic engineer: Both the color flow and power Doppler estimates are essentially derived from the same signal: the received signal from several pulse emissions by the scanner after removal of the stationary signal from the tissue by the clutter filter (5). The power Doppler estimator finds the power of the signal or alternatively, the power of the signal's spectrum. The color flow estimator essentially finds the mean frequency of the signal's power spectrum. In general, the noise in the signal will be added to the power Doppler estimate as the power of the signal and noise are summed. For the color flow estimator the mean frequency is found. Usually the power of the noise will be uniformly distributed over the spectrum, and its mean frequency will thus be zero, and will therefore have a smaller contribution than the estimate for the power Doppler estimator.

Theoretically, therefore, there is no obvious reason why power Doppler should be more sensitive than color Doppler. Basically the same data are used for the estimators, and physical circumstances, such as scattering strength, attenuation, transducer, etc., will influence both in the same way. A lot of postprocessing, e.g., cutoff frequencies in clutter filters, internal rejection ratios, and display methods, can influence how the estimates are presented. It is therefore important to compare the modes on the same scanner, patient, transducer, and time, as was done in our study.

Finally, Dr. Zhu states that differences in sensitivity as described in our report were the result of different frequency probes, and that variation in the quality of manufacturing may have also played a role. It should again be kept in mind that our study compared power and color Doppler within 6 machines, using factory and study settings. Within each machine the Doppler frequency remained the same for color and power Doppler, with both the factory settings and the study settings. Therefore, the different sensitivities obtained cannot be attributed to differences in Doppler frequency. The 6 machines came from 4 different companies, had different electronics, different settings, and different transducers, and used different Doppler frequencies. We observed a difference in Doppler sensitivity, but we are not able to conclude that this is due to a difference in Doppler frequency. The study was not designed to make comparisons among the machines, and we therefore anonymized them in the report. Likewise, we cannot conclude anything with regard to manufacturing quality.

The present correspondence illustrates how difficult it is to get rid of the dogma that power Doppler should be more sensitive than color Doppler. Dr. Zhu repeats this statement even though our study showed it not to be the case, even though the engineers manufacturing the equipment say it is not the case, even though it was not the case in an earlier study we reported (2), and even though Dr. Zhu himself has made the same observation: "Indeed, my colleagues and I have also noticed that color Doppler may appear more sensitive than power Doppler in detecting low blood signals. Nevertheless. . . ." When observations contradict theory, it is time to question the theory.

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Association between autoantibodies and neuropsychiatric manifestations of autoimmune disease: comment on the article by Lauvsnes et al

To the Editor:

We read with great interest the recent article by Lauvsnes et al (1), in which they suggested a correlation between antibodies to the NR2 subtype of N-methyl-D-aspartate receptor (anti-NR2 antibodies) in cerebrospinal fluid (CSF) and reduced hippocampal grey matter in patients with systemic lupus erythematosus (SLE) and patients with primary Sjögren's syndrome.

SLE and neuropsychiatric SLE (NPSLE) are multifactorial autoimmune diseases in which multiple autoantibodies can be detected in both serum and CSF (2). At least 20 brain-specific and systemic autoantibodies have been observed in the serum of patients with NPSLE, and different autoantibodies can be related to different clinical manifestations (2,3). Numerous studies have demonstrated a connection between anti–ribosomal P antibodies and neuropsychiatric manifestations, mainly psychosis and depression (4), although other studies have not shown this association.

We previously demonstrated binding of anti–ribosomal P antibodies to the hippocampus in mice injected intracerebroventricularly with this antibody (5). The mice exhibited depression-like behavior, olfactory impairment (5), and enhancement of brain–limbic structures as demonstrated by magnetic resonance imaging (MRI) (6). In addition, we demonstrated cognitive impairments and hippocampal inflammation in mice injected intracerebroventricularly with a specific idiotype of anti-DNA (7). Intracerebroventricular injection of antiphospholipid antibodies also correlates with behavioral changes in mice (8).

These and other studies suggest that antibody-mediated damage to the hippocampus and amygdala may play a role in the pathophysiology of NPSLE (9). Therefore, it would make sense to check a panel of autoantibodies in the CSF or serum of these patients and to perform a statistical analysis of clinical manifestations and MRI-detected brain morphology, including hippocampal atrophy.

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Reply

To the Editor:

We appreciate Drs. Kivity and Shoenfield's comments regarding our recent study regarding hippocampal atrophy and anti-NR2 antibodies in patients with SLE and patients with primary Sjögren's syndrome. The results of several studies published in the past several years have suggested an association between the presence of different autoantibodies and cerebral manifestations in autoimmune diseases. No specific marker has emerged as the major contributor to such an association, which indicates that several possible targets and signaling pathways may be affected.

Recently, Bravo-Zehnder and colleagues described how anti–ribosomal P antibodies gain access to the hippocampus in mice and interact with the neuronal surface P antigen (1). Previous studies in humans have shown somewhat conflicting results regarding the significance of anti–ribosomal P antibodies in autoimmunity (2,3) but also regarding other relevant autoantibodies such as anti-NR2 antibodies (4,5). There may be several explanations for this discrepancy, such as use of different assays, different matrices (CSF or blood),