Angle Independency of Fetal Speckle Tracking Echocardiography

genarians with and without moderate AS. To clarify, we did not check whether age is a prognostic factor in patients with moderate AS but inspected the mortality differences in older patients with and without moderate AS. Thus, the two papers do not contradict each other.

Edward Itelman, MD
Elad Maor, MD, PhD
Sheba Medical Center
Ramat Gan, and Tel Aviv University
Tel Aviv, Israel

REFERENCES

1. Saeed S, Rajani R, Tadic M, Parkin D, Chambers JB. Left atrial volume index predicts adverse events in asymptomatic moderate or severe aortic stenosis. Echocardiography 2021;38:1893-9.
2. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF, Dokainish H, Edvardsen T, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 2016;29:277-314.
3. Chew NW, Kong G, Ngiam JN, Phua K, Cheong C, Sia C-H, et al. Comparison of outcomes of asymptomatic moderate aortic stenosis with preserved left ventricular ejection fraction in patients ≥80 years versus 70-79 years versus <70 years. Am J Cardiol 2021;157:93-100.

https://doi.org/10.1016/j.echo.2022.02.013

Angle Independency of Fetal Speckle-Tracking Echocardiography: A Commentary Letter

Speckle-tracking echocardiography (STE) was introduced in 2004 to assess cardiac strain in adults. The assumed angle independency of STE can be a major advantage in the assessment of the fetal heart function in a highly motile fetus. Angle independency has been verified in in vitro studies,[1] but validation has never been performed during fetal life. Semmler *et al.*[2] were the first to investigate this objectively in a clinical setting. They found a significant difference between insonation angles and fetal left ventricular global longitudinal strain (GLS).[2] However, results should be interpreted with caution due to limitations in research design.

Their explanation is based on the anisotropic nature of B-mode ultrasound imaging. Depending on the acoustic characteristics of the myocardium, a random pattern of speckles appears. Multiple speckles within a certain area, known as kernels, have a stable location, and displacement can therefore precisely be tracked frame to frame during a cardiac cycle. Nevertheless, tracking can be hampered through low axial and lateral resolution, causing a reduced visualization of the full-thickness myocardium and leading to falsely low strain values (Figure 1).[3] Axial and lateral resolution are dictated by transmit frequency, bandwidth, and geometrics of the ultrasound probe. High frame rates and enhanced resolution should be improved by choosing the right ultrasound probe, optimizing sector width and depth, and appropriate use of magnification.[4] Less frequently considered features such as region of interest should also be optimized.[3]

However, even with the right settings, bias due to different insonation angles possibly exists. Within the oblique and perpendicular angles, the full thickness of the myocardium is visualized. However, in the up/down angle the full thickness of the myocardium is incompletely visualized and the kernels lie in the same axial alignment as the ultrasound beam. Alignment of the kernels and thin myocardial depiction could complicate adequate tracking. For the oblique and perpendicular angles, the thick myocardium and more spacing between the kernels ensure less influence of lower lateral resolution compared with the up/down angle (Figure 2). Unfortunately, Semmler *et al.* did not investigate the oblique and perpendicular angles as a reference.

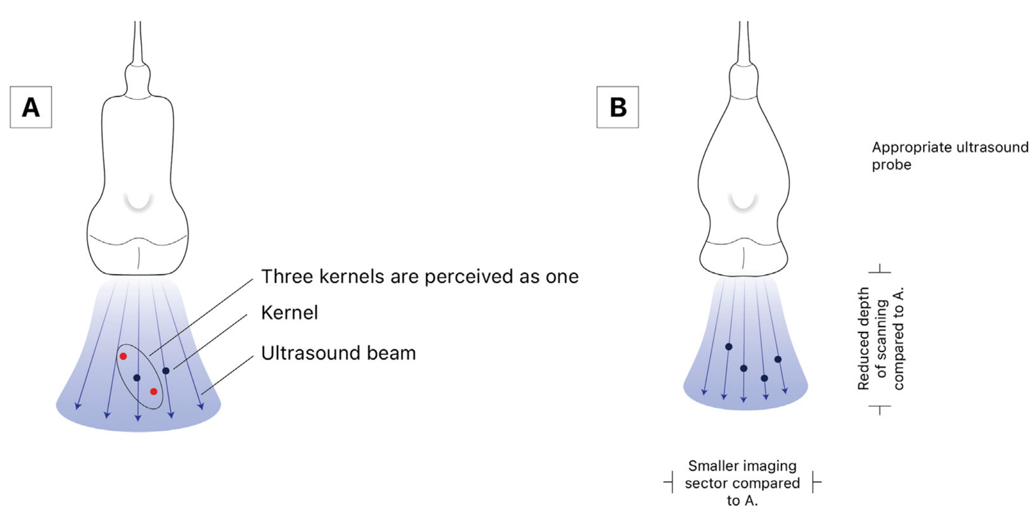

Figure 1 **(A)** Low lateral resolution. The ultrasound beams have a large distance between each other, making it impossible to distinguish the different kernels individually. **(B)** High lateral resolution. By optimizing the ultrasound settings (e.g., optimizing sector width, depth), the ultrasound beams become closer to each other. This allows the differentiation of every kernel individually, making STE more accurate.

Conflicts of Interest: None.

Reprint requests: Thomas J. Nichting, MD, Máxima Medical Centre, De Run 4600, 5504 DB Veldhoven, The Netherlands. (E-mail: *Thomas.Nichting@mmc.nl*).

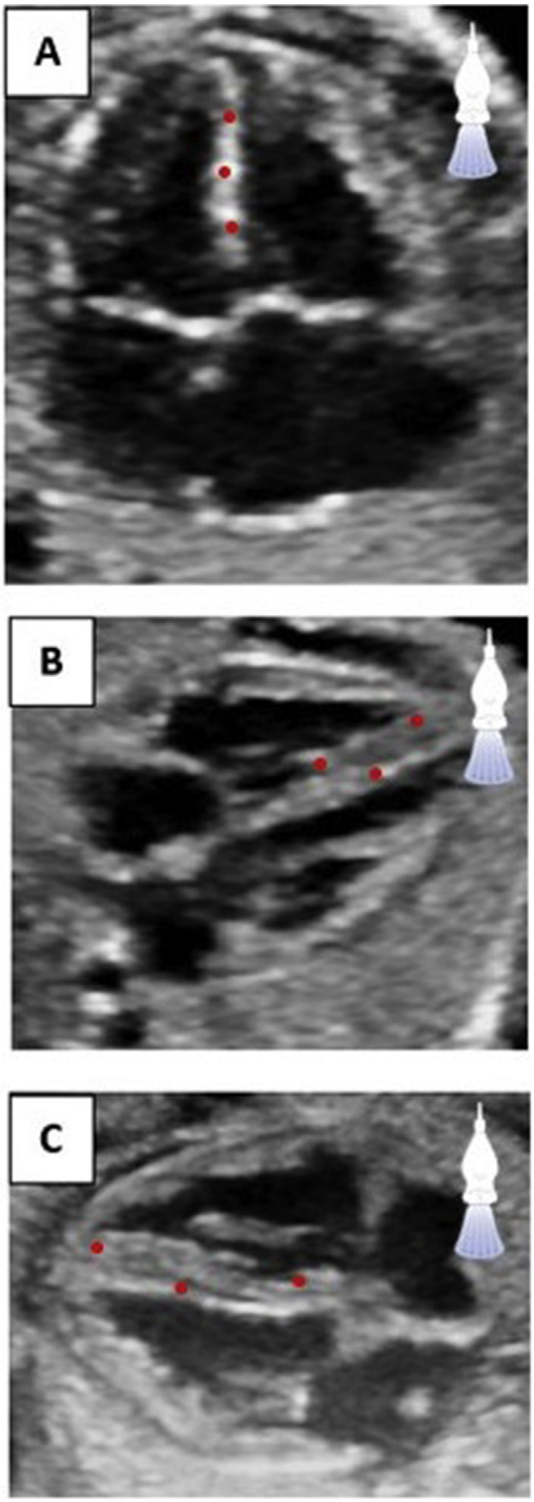

Figure 2 **(A)** Within the up/down angle of insonation, the myocardium is thinly depicted and the kernels are all in the same axial alignment compared with the ultrasound beams. It requires an extremely high resolution to be able to distinguish between the individual kernels (see also Figure 1). **(B, C)** The thickness of the myocardium is fully displayed in the perpendicular and oblique angles of insonation, allowing more kernels to be observed that are also aligned differently. Therefore, with a lower resolution it will still be possible to adequately distinguish between the individual kernels.

In addition, reference values for GLS have demonstrated the effect of gestational age on GLS values due to fetal heart maturation. With every week of increase in gestational age, GLS values increase accordingly.[5,6] However, the GLS means presented by Semmler *et al.* were based on a wide range in gestational ages. Differences in GLS values could therefore be due to normal variation between different gestational ages instead of an effect of insonation angles on GLS.

Most importantly, if significant differences have truly been found, the question remains whether it is clinically relevant. Reference values for GLS have a wide variation and vary between STE software programs. Reference values for Vitrea software (Canon Medical, Minnetonka, MN), as used by Semmler *et al.*, are not published. Therefore, it cannot be verified whether the presented GLS values lie within these reference values. Although reference values are vendor dependent, the mean values described by Semmler *et al.* fall within the boundaries of the known TomTec[5] (TomTec Imaging Systems, Munich, Germany) and Syngo software[6] (Siemens Medical Solutions, Malvern, PA) reference values. However, these reference values did not consider insonation angles. Nevertheless, the absolute mean variation for GLS between the different insonation angles is much smaller than the dispersion within the known reference values. This might suggest that the statistical differences are not truly clinically relevant.

In addition, Semmler *et al.* indicated a limited feasibility for making appropriate ultrasound images at different insonation angles within a subject. In only 62% of the subjects did they manage to obtain good-quality ultrasound images for all insonation angles and frame rates.[2]

In conclusion, more research needs to be performed on the actual effect of insonation angles on GLS before STE can be characterized as an angle-dependent technique. Theoretically, the preference would be the oblique and perpendicular angles due to the smallest effect of poor resolution. In future research, predefined angles, uniform image acquisition, and correction for gestational age are needed. However, even if differences between insonation angles exist, clinical relevance can be questioned.

Thomas J. Nichting, MD
Chantelle M. de Vet, MD
Myrthe van der Ven, PhD
Daisy A.A. van der Woude, MD, PhD
Department of Gynaecology and Obstetrics
Máxima Medical Centre
Veldhoven, The Netherlands
Department of Electrical Engineering
Eindhoven University of Technology
Eindhoven, The Netherlands
Eindhoven MedTech Innovation Centre
Eindhoven, The Netherlands

Ruud J.G. van Sloun, PhD
Department of Electrical Engineering
Eindhoven University of Technology
Eindhoven, The Netherlands
Eindhoven MedTech Innovation Centre
Eindhoven, The Netherlands

S. Guid Oei, MD, PhD
Department of Gynaecology and Obstetrics
Máxima Medical Centre
Veldhoven, The Netherlands

Department of Electrical Engineering
Eindhoven University of Technology
Eindhoven, The Netherlands
Eindhoven MedTech Innovation Centre
Eindhoven, The Netherlands

Noortje H.M. van Oostrum, MD, PhD
Department of Gynaecology and Obstetrics, University Hospital Ghent (N.H.M.v.O.), Gent, Belgium

Judith O.E. H. van Laar, MD, PhD
Department of Gynaecology and Obstetrics
Máxima Medical Centre
Veldhoven, The Netherlands
Department of Electrical Engineering
Eindhoven University of Technology
Eindhoven, The Netherlands
Eindhoven MedTech Innovation Centre
Eindhoven, The Netherlands

REFERENCES

1. Amundsen BH, Helle-Valle T, Edvardsen T, Torp H, Crosby J, Lyseggen E, et al. Noninvasive myocardial strain measurement by speckle tracking echocardiography: validation against sonomicrometry and tagged magnetic resonance imaging. J Am Coll Cardiol 2006;47:789-93.
2. Semmler J, Day TG, Georgiopoulos G, Sharland G, Charakida M, Simpson JM, et al. Fetal speckle-tracking: impact of angle of insonation and frame rate on global longitudinal strain. J Am Soc Echocardiogr 2020;33:1141-11462.
3. Pavlopoulos H, Nihoyannopoulos P. Strain and strain rate deformation parameters: from tissue Doppler to 2D speckle tracking. Int J Cardiovasc Imaging 2008;24:479-91.
4. DeVore GR, Polanco B, Satou G, Sklansky M. Two-dimensional speckle tracking of the fetal heart: a practical step-by-step approach for the fetal sonologist. J Ultrasound Med 2016;38:1765-81.
5. Oostrum NHM, Vet CM, Clur SB, van der Woude DAA, van den Heuvel ER, Oei SG, et al. Fetal myocardial deformation measured with 2D-STE: longitudinal prospective cohort study in 124 healthy fetuses. Ultrasound Obstet Gynecol 2021; https://doi.org/10.1002/uog.24781.
6. Lee-Tannock A, Hay K, Gooi A, Kumar S. Global longitudinal reference ranges for fetal myocardial deformation in the second half of pregnancy. J Clin Ultrasound 2020;48:396-404.

https://doi.org/10.1016/j.echo.2022.02.013

Angle Independency of Fetal Speckle-Tracking Echocardiography: Response

Response of the Authors:

We thank Dr. Nichting and colleagues for their interest in our paper. With respect to possible explanations of the results we reported, as we stated in our paper, the anisotropic nature of B-mode ultrasound "could be a possible explanation for the degree of angle dependence of the GLS [global longitudinal strain] values in our data."[1] Given the semiautomated nature of the speckle-tracking software, the user has little insight into the processes in the background, so assertions about the reasons during fetal life remain somewhat speculative. The angle independency referred to by Nichting and colleagues is from animal and human studies[2] and confirmed angle independency to the extent that both apical four-chamber and short-axis views correlated with sonomicrometry. In postnatal life, the four-chamber view is limited by the sonographic window, so different projections of the four-chamber view are technically very difficult or impossible.

We agree entirely that probe selection, sector width optimization, and the other measures described are important to optimize. In the up/down projection, the visualization of the full myocardial thickness will depend on lateral resolution. This projection is the one that is used during postnatal life for technical reasons as outlined above and for which the most validation data exist. We are not certain what is meant by not examining oblique and perpendicular angles as a reference. For the assessment of the effect of the insonation angle on GLS, apex up/down was selected as the reference group to compare its GLS values with those of apex oblique and apex perpendicular. In our paper, the measured GLS in each of the projections for the same fetus during the same study is presented and clear trends emerge, irrespective of whether a high frame rate or low frame rate setting was used.

The method of analysis employed in our paper compared the results of GLS within the same fetus and accounted for the gestational age of the measurement, and we do not accept that the differences observed are due to normal variation between different gestational ages. Essentially, the comparisons within each fetus are being analyzed.

With respect to clinical relevance, our study only included fetuses with normal cardiac structure and function. We did not set out to assess disease states or to look at predictive value of any measures. In clinical practice, no fetal cardiology guideline to date has included routine use of speckle-tracking, and we agree with the comments about vendor dependency of normal ranges. Many studies, however, are using speckle-tracking as a research tool to examine subclinical changes in myocardial function in different cohorts. One of the key points of our publication is that the design of prospective studies should take account of potential angle dependency of speckle-tracking measurements in their design, particularly with respect to the image acquisition protocol.

John Simpson, MD, FRCP
Department of Congenital Heart Disease
Evelina London Children's Hospital
London, United Kingdom

Marietta Charakida, MD, PhD
Division of Imaging Sciences and Biomedical Engineering
King's College London
London, United Kingdom

Janina Semmler, MD
Department of Obstetrics Charité
Universitätsmedizin
Berlin, Germany

REFERENCES

1. Semmler J, Day TG, Georgiopoulos G, Sharland G, Charakida M, Simpson JM, et al. Fetal speckle-tracking: impact of angle of insonation and frame rate on global longitudinal strain. J Am Soc Echocardiogr 2020;33:1141-11462.
2. Amundsen BH, Helle-Valle T, Edvardsen T, Torp H, Crosby J, Lyseggen E, et al. Noninvasive myocardial strain measurement by speckle tracking echocardiography: validation against sonomicrometry and tagged magnetic resonance imaging. J Am Coll Cardiol 2006;47:789-93.

https://doi.org/10.1016/j.echo.2022.03.011

Conflicts of Interest: None.

Reprint requests: Professor John Simpson, MD, FRCP, Evelina Children's Hospital, Department of Congenital Heart Disease, Westminster Bridge Road, London SE1 7EH, United Kingdom. (E-mail: *john.simpson@gstt.nhs.uk*).