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Ultrasound

White paper

Dynamic quantification of mitral regurgitation

Philips AI-powered 3D Automated Color Flow Quantification (3D Auto CFQ)

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Overview

This novel automated 3D color flow quantification tool provides an important measurement for mitral valve regurgitation assessment.

Background

Mitral regurgitation (MR) is the most common valve disease in the USA and China and the second most common in Europe.[1–3] For diagnosis, the severity of MR has been directly associated with patient prognosis.[4,5] Echocardiography is the most widely used imaging method to evaluate the mitral valve (MV).[6,7] The American Society of Echocardiography (ASE) recommends an integrated approach that incorporates quantitative, semi-quantitative and qualitative parameters to assess MR severity. This is because MR severity can have low reproducibility with significant disagreement across readers.[8] For example, patients in the Acorn Clinical Trial[9] were enrolled for significant MR. However, the core laboratory analysis evaluated 41% of patients as having moderate MR or less. The absolute measurements of effective regurgitant orifice area (EROA) and regurgitant volume (RVol) are the strongest MR predictors for outcomes.[7] The proximal isovelocity surface area (PISA) method is the most popular method for measuring EROA and RVol in routine clinical practice. However, the ASE recognizes that there are several limitations with the PISA method.[7] The 2D PISA method assumes a single, circular orifice that is constant across all of systole.[8] Three-dimensional (3D) echocardiography can provide additional information to supplement current methods for assessing regurgitation severity;[4,5] however, even 3D adaptations of PISA treat the orifice area with a circular calculation and can suffer from issues with reproducibility and correlation.[10] The Philips novel color flow quantification tool based on 3D echocardiography overcomes some of the PISA limitations in MR assessment.

Philips 3D Automated Color Flow Quantification (3D Auto CFQ)

The 3D Auto CFQ application provides automated quantification of MV RVol, which is one of the strongest outcome predictors[7], and peak flow rate from 3D color flow (3D CF) images acquired during transesophageal echocardiography (TEE) examinations **(Figure 1)**. This novel application uses a known fluid dynamic flow model adapted to acquired color information. This allows quantitative assessment of mitral valve leakage during systole. The 3D Auto CFQ application leverages artificial intelligence-powered Philips 3D Auto MV auto-segmentation technology to create an accurate and reproducible model of the mitral valve, which is then used as an input to the 3D Auto CFQ fluid dynamic flow model that quantifies the mitral regurgitation.

3D Auto CFQ uses 3D color rather than 2D to address the spatial complexities seen in MR. The 3D Auto CFQ application was developed to evaluate the regurgitant flow at every frame in systole to consider the temporal dynamics of MR. At the core of the 3D Auto CFQ algorithm is a complex fluid dynamic model of an incompressible fluid (blood) traveling through an irregular-shaped (i.e., non-round) orifice. The behavior of this model was confirmed through traditional computational fluid dynamics and found to match very well.

Image acquisition

Accurate quantification of MR using 3D Auto CFQ begins with the acquisition of a 3D color echo clip. 3D Auto CFQ computes the dynamic temporal changes in flow over systole; therefore, a volume rate of 20 Hz or more is required. Philips recommends the X8-2t transducer, which is capable of single-beat 3D color volumes over 20 Hz, and even higher frame rates with multi-beat acquisition, if indicated. Furthermore, high color scale (60 cm/s minimum, with ≥70 cm/s recommended) is necessary since the fluid dynamic model uses all of the velocities within the regurgitation to compute flow volume. A data adequacy indicator **(Figure 2)** for volume rate and aliasing velocity is provided for the user.

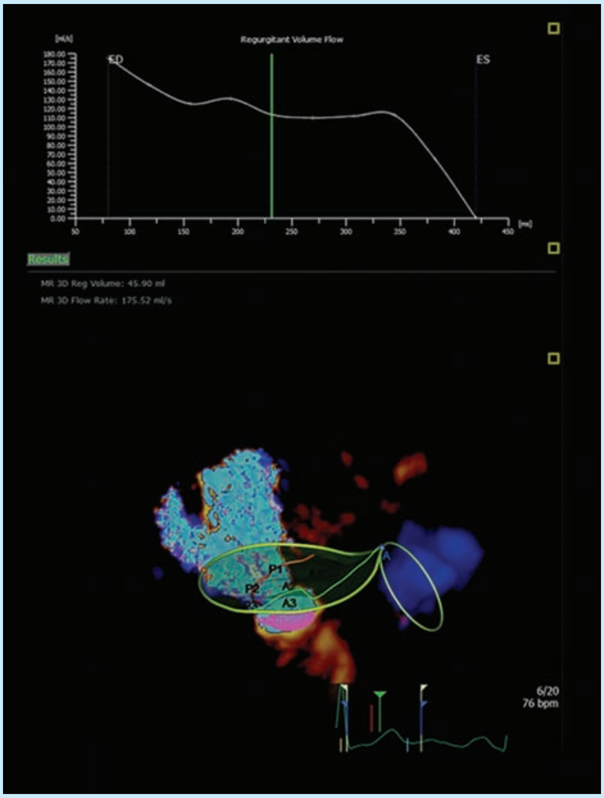

Figure 1 Example results of Philips 3D Auto CFQ showing dynamic temporal flow and three-dimensional flow characteristics.

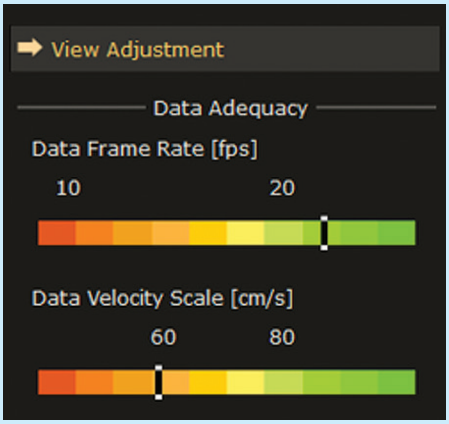

Figure 2 Data adequacy indicator from "view adjustment" step showing frame rate and velocity scale of the loaded 3D color data set.

3D Auto CFQ workflow steps

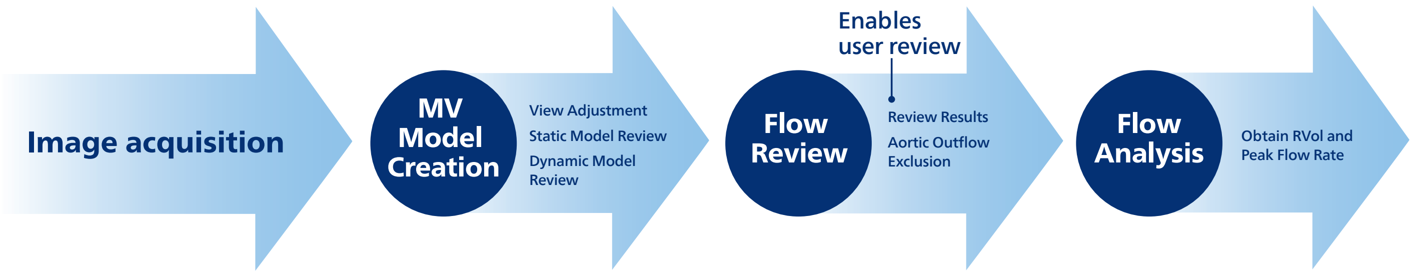

Figure 3 Flow chart demonstrating the 3D Auto CFQ application workflow and functional steps.

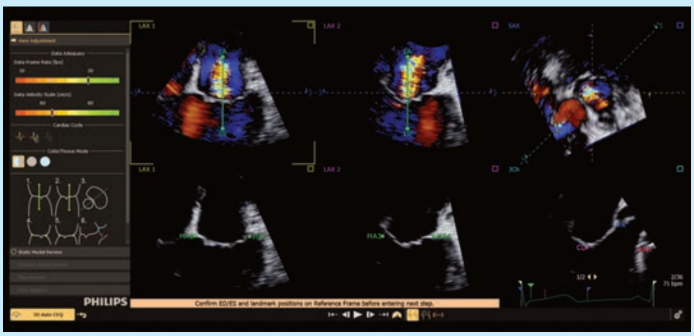

Figure 4 User interface. In the initial "View Adjustment" step, the software provides tools for the alignment of the volume, positioning of the key points and cardiac timing adjustments as inputs to create the static MV model.

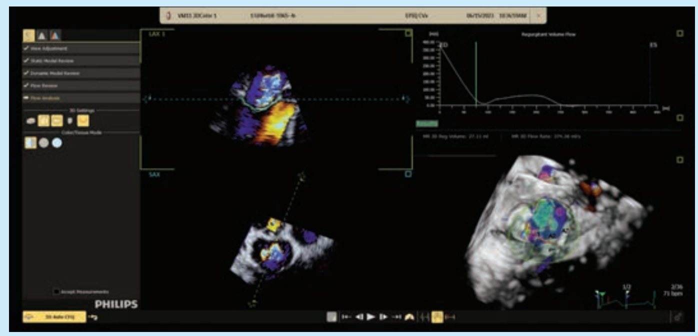

Figure 5 Final result page showing computed results, a graphical illustration of regurgitant flow over time and visual overlays of the flow model on the 2D and 3D echo images.

Workflow

The 3D Auto CFQ application workflow follows the chart depicted in Figure 3 (above). The user begins in "View Adjustment" with automated landmark detection of the mitral valve within the 3D greyscale volume to create a dynamic model of the mitral valve **(Figure 4)**. The technology used in this step is the same as in 3D Auto MV.

In the following two workflow steps, the anatomical information of the mitral valve is refined in the "Static Model Review" and "Dynamic Model Review" to look for the location of the likely orifice, which serves as a starting point for the 3D Auto CFQ algorithm to compute regurgitation.

The created valve model serves as an input to the 3D Auto CFQ algorithm itself **(Figure 3)**. The intersection of the 3D color data and the leaflet surface of the mitral valve model is used to determine the irregular shape of the regurgitation orifice.

In "Flow Review," the user reviews the fit of the overlay generated by 3D Auto CFQ with position and shape of the adequate isovelocity surface seen in the 3D CF volume across all frames. If the user is not satisfied with the 3D Auto CFQ detection, the user can either go back to the "View Adjustment," "Static Model Review" and/or "Dynamic Model Review" steps and further refine them or decide to discard the 3D Auto CFQ analysis **(Figure 3)**. Finally, if the user agrees with the detected overlay, the user can proceed to the final results in the "Flow Analysis" step **(Figure 5)** which provides:

- Regurgitant volume in ml (RVol [ml])
- Peak flow rate in ml/s
- Graphical illustration of the regurgitant flow over time

Algorithm explanation

While a physics equation to model irregular flow traveling through an irregular orifice does not exist, simulations to model the laminar flow of liquids moving through a small, circular pinhole orifice are well-known and used in many computational flow applications.[11,12] 3D Auto CFQ takes advantage of this simple, generic pinhole model by fitting the detected irregular orifice with a grid of these known pinhole flow models **(Figures 6 and 7)**. The algorithm then generates a hypothetical model of flow velocities based on the sum of all the pinhole flows in the given orifice input.

The flow model is converted into a virtual Doppler image using ultrasound physics (with appropriate projection along the transducer's axial dimension). This virtual Doppler image is compared to the true color Doppler image in the 3D CF dataset. Based on the outcome of this comparison, the model is updated and reiterated with different pinhole sizes and flows to get the best fit between the acquired velocities and the generated model **(Figure 7)**.

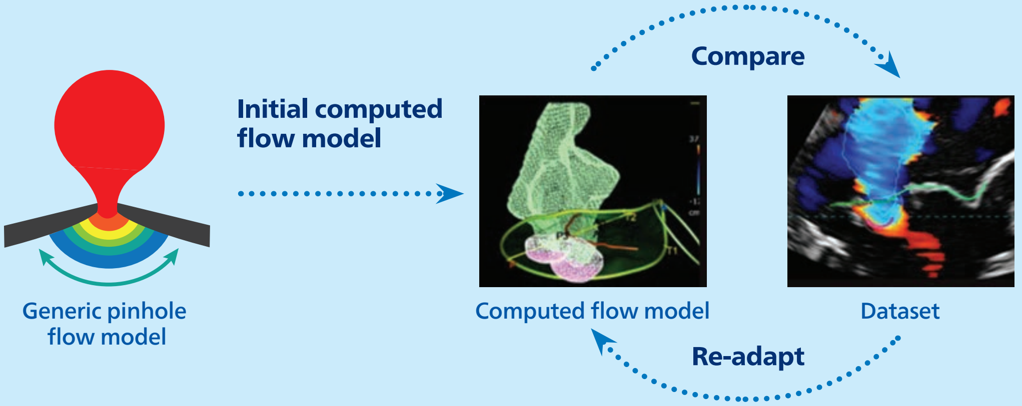

Figure 6 The solution is to create a flow model that is comprised of many small pinhole flow orifices that morph and adapt into the size and shape of the actual irregular orifice in the echo image.

Since the behavior of these pinhole orifices is known, the combined flow is simply the convolution (summation) of the contribution of all these pinhole flows. If the predicted velocity profile of the model matches the velocity profile in the acquired echo dataset, we can be confident that the computed volume in the model matches the flow volume seen in the echo image.

With a sufficient match, 3D Auto CFQ can determine the resulting regurgitant flow rate for the given frame, as the flow contribution for each individual pinhole is known and summed together to report the volume. This process is repeated for every frame included in the analysis across systole. In each frame, the size and shape of the regurgitant orifice is not assumed but is generated by this iterative loop between the model and the 3D CF data.

In Figure 7, (A) is the original acquired 3D color Doppler dataset of regurgitation showing the regurgitant flow hemisphere underneath the mitral valve. (B) is an initial guess for the flow model made with a single pinhole. The flow model generates a virtual Doppler image based on that single pinhole. The virtual image is compared back to (A) but does not align with the color Doppler image. In (C), additional pinholes are added to the flow model and create the subsequent virtual Doppler image. In this case, the iterative comparison back to (A) shows a good match, and the volume flow is calculated from the final flow model.

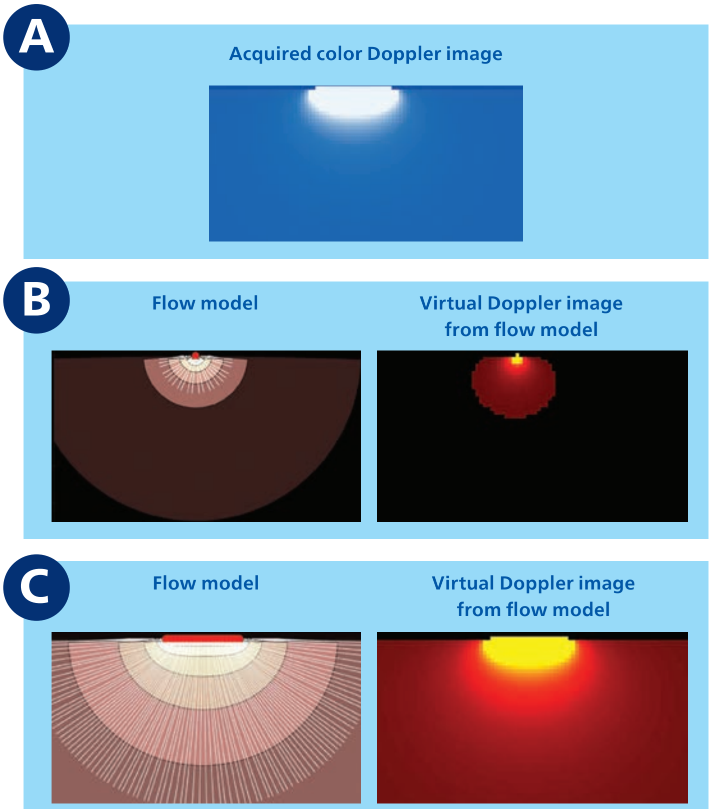

Figure 7 Simplified example of 3D Auto CFQ algorithm.

Validation study

As part of the validation of the algorithm, a retrospective study was conducted to evaluate the performance (agreement) of 3D Auto CFQ to quantify mitral valve regurgitant volume from 3D TEE clips (averaged across three reviewers) compared to cardiac magnetic resonance (CMR) assessment (ground truth) for the same subject as acquired within 24 hours of the echo imaging.

A total of 52 TEE cardiac clips were used for RVol quantification with the 3D Auto CFQ software by the three reviewers. The primary endpoint in the study was defined as Bland-Altman agreement assessed between CMR-based mitral valve regurgitant volume (ground truth) and automated 3D Auto CFQ outputs obtained from the average of the three reviewers **(Figure 8)**.

The maximum limit of agreement (Δ=±65 mL) was determined a priori from literature[17] based upon the acceptable comparison of RVol between the current standard of care 2D PISA and CMR. The mean bias limit (±19.2 mL) was also established from the same literature from 2D PISA and CMR.

The results of the study, in fact, showed better agreement of 3D Auto CFQ (RVol) with CMR than PISA (RVol) with CMR. Furthermore, 3D Auto CFQ met the bias limit. The results also demonstrated clinically reasonable, relevant and meaningful performance of the 3D Auto CFQ software, which supports clinician assessment of mitral valve regurgitant volume during a cardiac TEE exam. Specifically, success on the primary endpoint of 3D Auto CFQ agreement with CMR indicates that the safety and effectiveness of the proposed software is acceptable and aligns with the reported agreement comparing echocardiology to CMR for mitral regurgitation evaluation.

The study also assessed interobserver agreement for the 3D Auto CFQ software **(Figure 9)**.

Interclass correlation (ICC) values greater than 0.9 indicate excellent reliability. The agreement between reviewers was reported for RVol and peak flow rate with interviewer reliability of 0.968 (95%CI 0.96, 0.98) and 0.914 (95% CI 0.88, 0.94), respectively. The results showed consistency and high agreement among the reviewers when utilizing 3D Auto CFQ software.

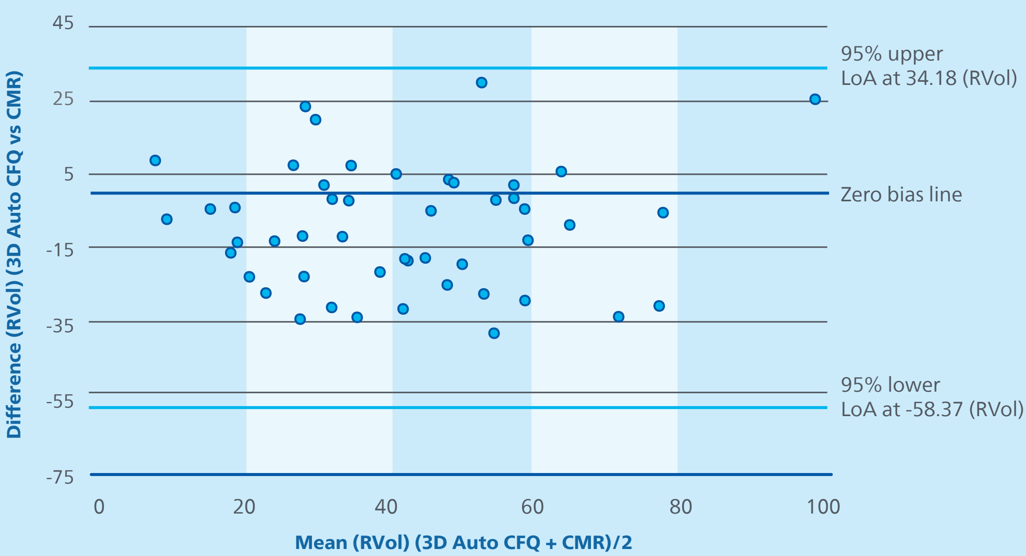

Figure 8 Bland-Altman plot from validation study between 3D Auto CFQ and CMR. The maximum limits of agreement (Δ=±65 mL) and the bias limit (±19.2 mL) were determined from various literature comparing 2D PISA and CMR.

Measurements	N	ICC (3,k) (95% CI)
3D CFQ Automated RVoL(ml) (across three reviewers)	52	0.968 (0.96, 0.98)
3D CFQ Automated Peak Flow rate (across three reviewers)	52	0.914 (0.88, 0.94)

Figure 9 Inter-reviewer reliability of CFQ RVol across three reviewers.

Conclusion

Philips 3D Auto CFQ is designed to address the shortcomings inherent in current clinical practice for evaluating MV regurgitant volume. By making no assumption on orifice size and shape, and by computing flow on all systolic frames, a reproducible quantification of mitral regurgitation volume can be obtained.

This is supported by studies comparing 3D Auto CFQ volume outputs to CMR, as well as studies showing reduced variability across users.[13,14] The intuitive workflow and user interface provide users with a novel tool for use in clinical practice on a wide range of patients.

Frequently asked questions

Why are the obtained regurgitation volumes lower than what I get in 2D PISA?

3D Auto CFQ usually provides regurgitation volumes lower than in 2D PISA because it is evaluating all frames of the regurgitation. PISA computes the EROA on a single frame with the largest jet and assumes the same EROA across systole. Since PISA usually obtains higher RVol values than CMR, this is in line with our findings of correlation between 3D Auto CFQ and CMR.

What does the purple mesh overlay represent?

This is the location of detected flow convergence. Flow convergence is an area of the mitral regurgitation in the ventricular side, where blood is traveling at the same velocity. In PISA, this is assumed to be a hemispherical shape, but in reality, the convergence is irregular and dynamic. The correspondence between the mesh and the color Doppler is used by the user to confirm that the flow was properly detected.

How is this different from 3D PISA or eSie PISA?

In 3D PISA solutions, the orifice area can be measured in 3D, which can provide a more accurate measure of the orifice size. However, regardless of the shape, the area of the orifice is still assumed to be a circle and is still computed on one frame.

Is there a gold standard for measuring mitral regurgitation?

While there is no universally agreed-upon gold standard for measuring mitral regurgitation, CMR is perceived as the best method available. This is why CMR was selected as the ground truth for the 3D Auto CFQ validation study.

How do I avoid LVOT flow in the RVol calculation?

In the final “Flow Analysis” step, if a user notices LVOT being detected as part of the regurgitant volume in the flow convergence area, the aortic exclusion capability in the previous “Flow Review” step can be used to remove the LVOT contribution from the regurgitation volume.

Does 3D Auto CFQ work on multiple jets? Eccentric jets?

The 3D Auto CFQ validation study included patients with multiple jets and eccentric jets as part of the study.

Does 3D Auto CFQ work on valve replacements or MitraClip patients?

The 3D Auto CFQ validation did not have images of patients with replacement valves or devices available in the study.

Are there peer-reviewed papers associated with this algorithm?

Two peer-reviewed papers have been published using the underlying 3D Auto CFQ algorithm.

Militaru, et. al. (2019)[13] demonstrated correlation of the 3D Auto CFQ flow quantification algorithm compared to 2D PISA RVol measured by TEE and TTE, as well as comparison to CMR RVol. The 3D Auto CFQ RVol showed far better correlation to CMR (ICC=0.86) than 2D PISA by TEE or TTE (ICC=0.69 and 0.66, respectively).

Singh, et al. (2022)[14] similarly showed that the 3D Auto CFQ measurement had less variability across users as compared to the 2D PISA method across MR subtypes. The authors found that the automatically generated temporal flow curves from 3D Auto CFQ were indicative of MR mechanism. Primary MR cases, which are caused by prolapse or flail, demonstrated a single peak, non-holosystolic duration flow pattern. Functional MR cases demonstrated characteristic early and late peaks of flow in systole with a quiescent midsystolic flow pattern. These findings are supported by previous studies showing distinct temporal patterns according to the etiology of MR.[15,16]

How is the reproducibility of CFQ?

The validation study showed excellent agreement across the three reviewers for evaluation of RVol and peak flow rate with ICC reliability of 0.968 (95%CI 0.96, 0.98) and 0.914 (95% CI 0.88, 0.94), respectively. This was also supported by Singh et al.,[14] which showed good ICC values using a preliminary version of the algorithm without the mitral valve tracking component.

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