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Development of screening echocardiogram for detection of asymptomatic left ventricular dysfunction

Irmina Gradus-Pizlo, School of Medicine, UC Irvine, Irvine, CA. U.S.A.
Kunal Agrawal, Department of Psychological Sciences, Purdue University, West Lafayette, IN. U.S.A.
Edward Delp, School of Electrical and computer Engineering, Purdue University, West Lafayette, In. U.S.A.
Zygmunt Pizlo, Department of Cognitive Sciences, UC Irvine, Irvine, CA. U.S.A.

Abstract
Clinical data about heart failure make it clear that there is a need to develop a limited echocardiogram assisted by automated functions as a screening tool to identify people who have asymptomatic left ventricular dysfunction and who can potentially benefit from proven therapies to prevent the development of symptomatic HF. Our preliminary tests show that an abbreviated version of an echo consisting of only 6 views can provide enough information for the binary screening. Six expert echo readers achieved near-perfect performance in identifying normal vs. abnormal echoes using 6 views, as compared to the diagnosis based on the full echocardiogram. The ground truth about the geometry of the heart was provided by one expert echo reader in the form of drawings and measurements. The drawings were used as a prior in a computational model that extracts the contour of the left ventricle as the shortest path in a log-polar (complex log) representation of the ventricle. This model may represent the first step in the development of an automated function for screening echocardiogram.

Introduction

Heart failure (HF) affects 5.5 million Americans, and the cost of treating symptomatic HF is estimated to be $40 billion a year [1,2]. HF is the inability of heart to pump enough blood to satisfy the need of the body, or to do it under increase filling pressures. In most patients HF develops as a slowly advancing disorder and is a result of progressive heart damage by diseases like diabetes, hypertension and atherosclerosis leading to heart attacks. There is an estimated 30 million Americans who have early stages of asymptomatic left ventricular (LV) dysfunction. Patients are not aware of this problem due to lack of recommended screening and once HF is established, the mortality is 90% in 10 years. Early detection of asymptomatic LV dysfunction could produce significant benefits for patients and for population health [3,4].

Echo examinations are considered to be a gold standard in evaluation of cardiac function. Clinically used diagnostic echocardiogram has at least 50 to 100 views, takes 30 minutes to acquire, 15 minutes to perform measurements and 15 minutes to interpret. Skilled echocardiographer can interpret 5-6 studies per hour. A standard echocardiogram costs ca. $500-$1,000. There are 20 million echoes performed each year in the U.S.A. for a total current cost of 10-20 billion a year but there is no systematic screening of population at risk.

As will be shown in the next section, most patients with early stages of HF cannot be diagnosed by their physician unless a specific tool, such as an echo is used. A visit to a general practice doctor usually does not reveal a HF problem. These patients look good and general medical examination will not lead to the primary doctor's recommending a cardiology consult. This is similar to other health risks such as breast or colon cancer. However, unlike cancer risks which already have widely used screening, HF still does not have a comparable tool.

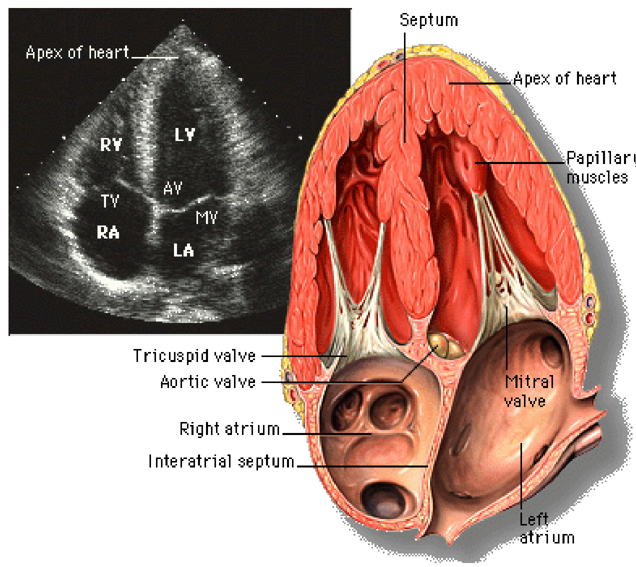

Figure 1. Apical 4 chamber view of the heart. Right atrium (RA) receives returning venous (blue) blood from the body, fills the right ventricle (RV) which pumps blood to the lungs for oxygenation. Left atrium (LA) receives oxygenated (red) blood from lungs, fills the left ventricle (LV), which pumps blood to the body. Early changes in chambers size and function may be detected by echocardiography even before patient develops symptoms of shortness of breath, fatigue or swelling of legs.

Scope of the Challenge.

Figure 1 shows a schematic view of the heart along with a corresponding echo view. Figure 2 shows one frame of a four view echo display called a "quad" view. Now look at the movie (video1), which shows a 4-view echo of a patient who was on a heart transplant list. When you just looked at this 47yr old patient, you would not say that she had advanced cardiac dysfunction. If we cannot rely on person's general appearance in the advanced stage of disease imagine the difficulty to diagnose asymptomatic disorder. The patient's activity is usually limited, but at the early stages of cardiac dysfunction the patient may not even complain simply because the patient has been adapting to the progression of the disease for years. Unfortunately, physical examination is also not perfect and even cardiologists fail to detect 43% of findings that have been classified as “major” based on auscultation [5].

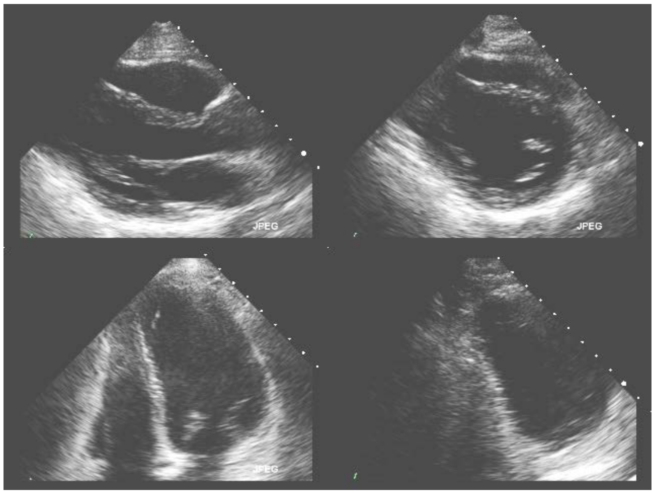

Figure 2. One frame of a four view echo display called a “quad” view. Two top images show long and short axis view of the heart obtained from echo probe placed in left side of sternum on patient’s chest (parasternal views). Two bottom images show four chambers and two chambers view of the heart obtained from echo probe placed close to the apex of the heart (apical views).

Figure 3 summarizes the timeline of the disease progression. In most cases the disease develops slowly, over decades. At the same time, there is proven, guidelines recommended, inexpensive medical therapy with beta blockers and ACE Inhibitors, which will slow the disease progression [6-9]. But there is no method to screen the population at risk for presence of asymptomatic LV dysfunction.

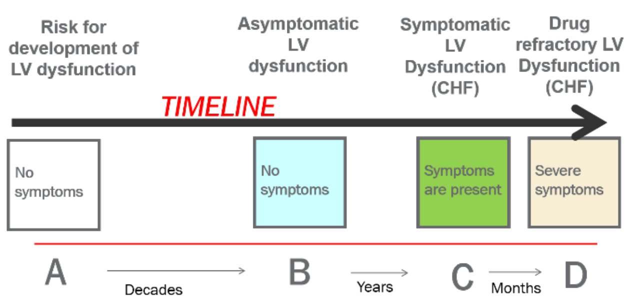

Figure 3. Defining the population of patients with CHF [10].

There are estimated 60 million Americans in stage A, which means asymptomatic patients who have one or more risks for development of LV dysfunction. Additionally, there are 33 million Americans in stage B, which are patients with asymptomatic LV dysfunction. These patients have the disease, but they have no symptoms or their symptoms are not diagnosed. This group has significant 10-year mortality described by long term Framingham study as pictured on Figure 4 [11].

Using technical jargon, the disease is in the null space of the current medicine. As already pointed out, the development of the disease can be dramatically slowed down pharmacologically. The population that receives treatment under current guidelines is in stage C and D, with a total of over 6 million patients who are already very sick. These are the two groups whose care costs over $40 billion annually, with over half of these costs spent on > 1 million hospitalizations per year.

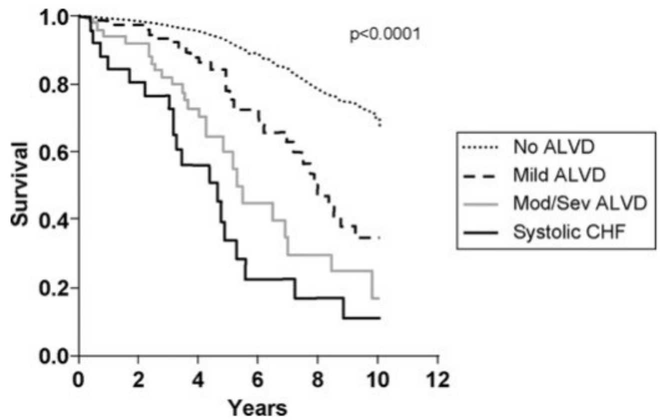

Figure 4. Kaplan-Meier curves for survival of patients with asymptomatic LV dysfunction (ALVD) compared with normal population and with patients with CHF.

Opportunity.

There is a need to screen large population of patients who are at risk of developing HF. Mortality for HF is 270 per 100 thousand people per year. Yet, there is no recommended screening despite the availability of noninvasive methods. Physical exam, ECG or blood work are not adequate for diagnosis of HF [12]. As a comparison, there is recommended screening for colon cancer with colonoscopy once you are 50 years old. Mortality of CC is 16 per 100 thousand people per year, which is 15 times lower than in HF [13]. Note also that colonoscopy, the screening method, is both expensive and invasive (not to mention the preparation).

Screening 30% of adult population will require additional 90 mln studies, likely repeated every 5-10 years. We identified 3 main barriers that would have to be overcome: workforce, cost and technology. The rest of this paper will propose ways to do it.

New Approach.

If 30% of US population (over 90 mln Americans) is screened every 5-10 years, there will be more than 10 mln screening echoes to interpret every year. With the current cost of $500-$1,000 per echo, HF screening will add significant cost to an already expensive care. But even more importantly, there will need to be increased number of echo technicians and echo readers to acquire and interpret them. These additional screening echoes will add more than 50% of echoes to an already existing 20 mln studies, annually. The only way to justify echo screening is to scale it down and automatize it, at least partially.

In order to introduce echo based screening tool, echocardiogram needs to be scaled down to small number of views. Acquiring such a screening echocardiogram should take about than 10 minutes to acquire, measurements should be assisted by a computational model, and the interpretation should focus only on providing a binary decision whether the screening echo is normal vs abnormal. The cost of screening echo should be less than $200.

Our preliminary experiment suggests that 6 views may be sufficient for screening. In addition to the 4 views shown in Figure 2, there should be two additional views, as shown in Figure 5. Parasternal long axis view with color Doppler interrogation of the mitral and aortic valve will provide information about key valvular function, and spectral Doppler through the mitral valve will provide information about the filling pressures of the left ventricle which is an important hemodynamic parameter.

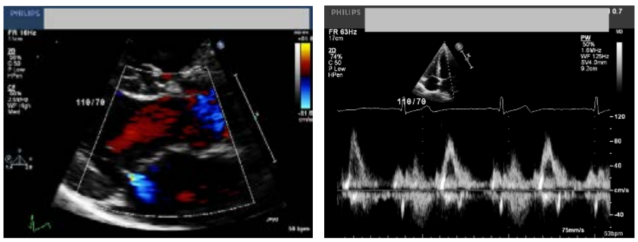

Figure 5. Two additional views for the 6 view screening echo.

One of us (IGP) randomly selected from the IU Health database of echocardiograms 50 normal and 50 abnormal echoes. Six views were extracted. Measurements were obtained from these views as part of initial interpretation. Five readers were asked to make binary decision whether echo was normal or abnormal based on visual assessment and then final decision after looking at measurements. Some of the readers had years of experience, others have been reading echoes for about a year or two. Across the 5 readers, 94% echoes were correctly classified based on visual assessment, and 98% correct when measurements were available. The average time of interpretation was less than 2 minutes per study. This experiment will be repeated with larger number of echoes and with realistic base rates of normal vs. abnormal. But already these results confirm our expectation that small number of views will be sufficient for screening the population at risk.

Towards an automated analysis of echocardiograms.

Look at the left ventricle (LV) in Figure 1. The 2D images are used to estimate 3D geometry of the LV throughout the heart cycle and characterize cardiac function. If the pumping function of the heart is normal, then the ratio of the maximum volume of LV to its minimum volume (referred to as ejection fraction) is in the range of 55 to 65%. What really matters is the volume of the blood that is pumped and the spatiotemporal geometry of the heart can be used to estimate it.

Look at Figure 6. The contour of LV drawn by an expert echo reader is shown in green and superimposed on contours extracted by a standard edge detection algorithm. Recall that the output of edge detection is a set of edge pixels – here shown in white. You see curves, but edge detection does not produce contours; only isolated pixels. The green contour was actually drawn on top of the raw image shown on top of Figure 6. The next movie (video2) actually shows a normal echocardiogram with superimposed contours drawn by an expert. The expert drew the contours on stationary images and she did not have in front of her the previous images and contours. This leads to some uncorrelated noise in the drawn contours due to noise in the motor system, as well as visual system. We will point out later in this paper that a computational model will not have a motor noise and the visual noise can be reduced because the model can use the information from all images. Once the contours are drawn, they are used to estimate the volume of LV using an approximation that assumes that LV is a truncated ellipse.

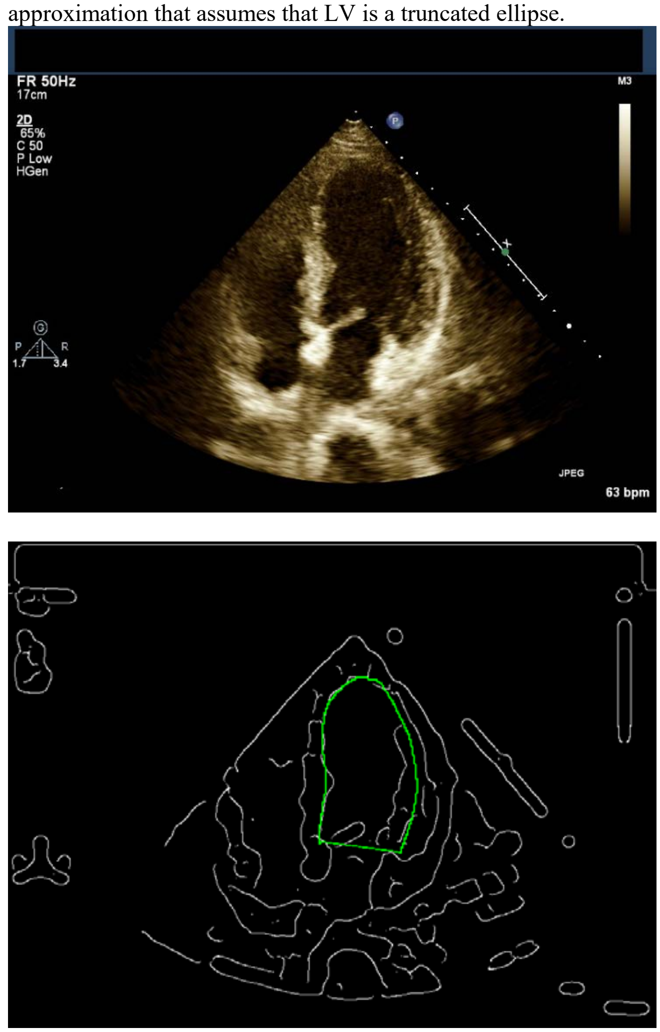

Figure 6. Top: one image from an echocardiogram. Bottom: ground truth superimposed on a standard contour extraction result.

Extraction of contours from images has received a lot of attention in computer vision literature [14-24]. It has also received attention in psychophysical literature [25-32]. Here we build on the model recently developed by one of us [33]. It is known that human observers can detect closed curves in noisy images very well. An example of a stimulus illustrating this is shown in Figure 7 labeled "retina." A pentagon, represented by a fragmented contour is embedded in 300 distractor pieces of contours. The stimulus was prepared in such a way that proximity of contours was not a useful feature allowing detection of the pentagon. Only smoothness, closure, and convexity could do the job. When the reader looks at this stimulus, she can easily see the pentagon. The pentagon is marked in red in Figure 7, labeled as "perceived contour". In fact, this perceived contour was produced by Kwon et al.'s model. The subjects in their experiment used a stylus to draw what they saw on a tablet. They tested 3 subjects. One of the subjects was naïve about the underlying hypotheses. Their experiment used both convex and concave polygons. The difficulty of the task was manipulated by adding a random jitter to the orientation of the edges representing the polygon. Performance of all 3 subjects was very similar and very good. This is not surprising: most visual functions are characterized by very small individual differences: We all see things the same way. Kwon et al.'s model was motivated by the known architecture of the primate primary visual area V1 [34].

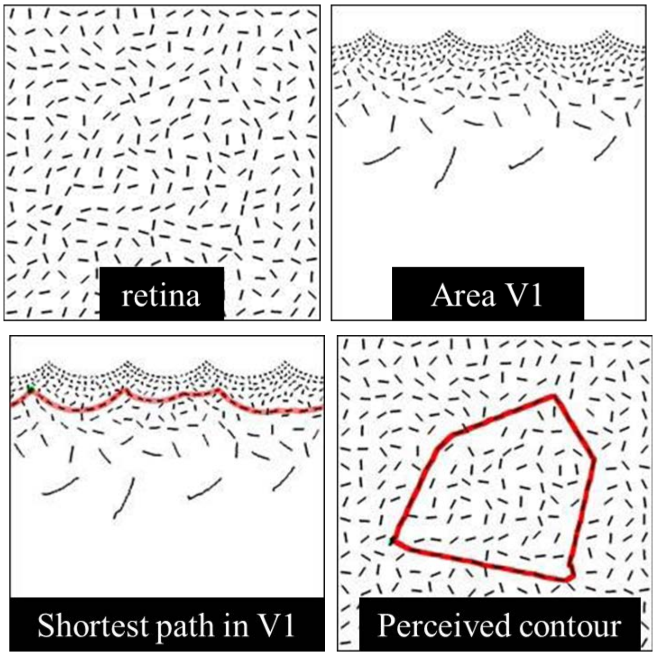

Figure 7. An illustration of how the shortest path in the complex-log representation corresponds to a smooth, convex and closed contour in the image (after [33]).

It is known that the distribution of cone receptors on the human retina is not uniform. More specifically, the distance between the neighboring cones is proportional to their eccentricity, which is the distance from the center of the retina. This proportionality is not perfect around the very center due to the finite size of the cone, whose diameter is 0.3 minutes of arc. So, there is high density of cones in the center of the retina, and the cones are sparser in the periphery. It follows that in order to see details, we orient the eyes in such a way that the image of the detail falls into the center of the retina. The retinal image is mapped onto area V1 in the occipital cortex and this map is distorted. One way to see why distortion is needed is to realize that it is economical to distribute the neurons in the volume of the brain approximately uniformly. So, what are the possible transformations from the known distribution of cones on the retina into a uniform distribution on the surface of V1? There is only one such transformation and it is called complex-log.

Consider the Cartesian coordinate system (x,y) on the retina and the corresponding polar coordinate system (r,φ). Now, instead of using a pair of real numbers (x,y) to represent a point, we will use a complex number $z=x+iy$, or in Euler notation $z=re^{i\varphi}$. If you take a complex logarithm, you get a complex-log representation corresponding to a complex plane: $\ln(r)+i\varphi$. So, the radius on the retina is transformed into its natural logarithm and the polar angle is expressed in radians. Complex-log map belongs to the family of conformal maps, which preserve local angles (but not curvatures) [35]. Figure 7, panel labeled "area V1" shows how the stimulus looks like in the complex-log representation. It is easy to realize that the complex-log map of a retinal stimulus depends on the position of the origin of the polar coordinate relative to the stimulus. So, the representation in V1 is not translation invariant. But it is scale and rotation invariant. Interestingly, when translation on the retina occurs, local angles are invariant, too. This means that any measure of smoothness of a contour that is based on local angles, will be translation invariant, too.

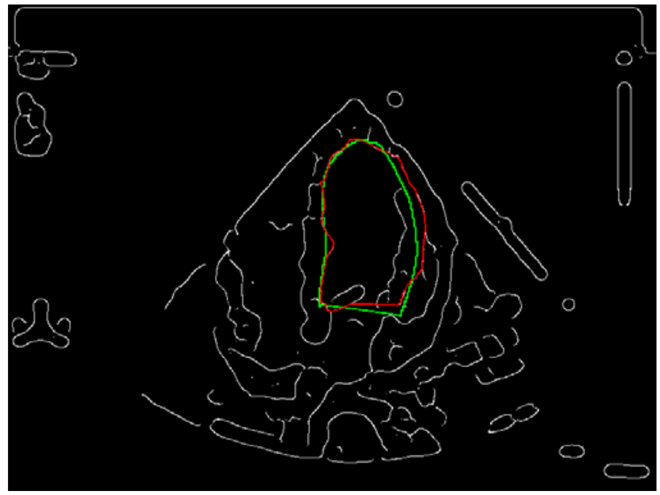

Figure 8. The ground truth from Figure 5 and superimposed model's contour that used the ground truth as a prior.

Next, note that the problem of integration of a fragmented closed curve on the retina translates into the problem of finding the shortest path in the complex-log representation. More precisely, it is the problem of the least-cost path where the cost evaluates the size of the interpolations and the size of turning angles. The shortest path problem can be solved optimally in a polynomial time. So, what looks like an NP hard problem on the retina is transformed into a P problem in the complex-log representation. Note that we are not claiming that P=NP. What we are saying is that a problem for which it is difficult to find a polynomial approximation in the retina has a natural polynomial approximation in the complex-log representation. Gestalt Psychologists have always claimed that a key to solving difficult problems is in finding the right representation [36]. Kwon et al.'s model is a good illustration of this claim. The panel "shortest path" in Figure 7, shows the shortest path between the left and right edges of the map labeled "area V1." Once the shortest path is found in the complex-log map, it is back projected to the retina and the result is shown in the panel labeled "perceived contour" (see [33] for details of the model and for the psychophysical tests).

Kwon et al.'s model is a model of how every human being sees contours in images. This is surely how a medical resident sees contours in the echocardiogram. By the time, the student finishes her cardiology fellowship with specialization in echocardiography, she will see the contours in the echo much more accurately. During the training, the cardiologists builds a mental model of the heart, and connects this model with the examples of echo images. At this point, we have a model of a naïve human observer and we improved the model's performance by using the expert's drawing as a prior. An example of how such a model compares to the ground truth drawn by an expert echo reader is shown in Figure 8.

The model starts with a standard edge detection applied to a blurred image. Then, it uses the center of LV as the origin and applies complex-log transformation. Then, it selects a starting point and solves the least-cost path. But the cost is now modulated in such a way that the path is biased towards the path representing the ground truth.

Figure 9 shows a number of images from an echo cycle with the ground truth and with the model's contour superimposed. In these simulations, the model used the ground truth as a prior only once, for the first image. For all subsequent images, the prior for image n+1, was the model's contour from image n. These are very preliminary results, but they are encouraging. Note that what is important is not that the contours are perfect, but that characteristics such as rejection fraction, derived from the contours are correct.

Future work.

There are a number of aspects of our model that have to be improved and worked out. First, is the automatic estimation of the center of LV. Second is the optimal choice of parameters for edge detection. Next, is the optimal choice of a cost function that combines the contours from image n+1 with the prior from image n. Next, is the smoothing of the resulting contour. Finally, we will need to build a statistical model of the prior that can be applied to the first image automatically. This prior will be derived from a large data based of the contours drawn by expert echo readers.

Conclusions.

There are two main contributions in our paper. First, we call the attention of the medical and imaging communities to the need for developing a screening tool for asymptomatic cardiac dysfunction. This screening will be based on a reduced echo represented by 6 views. This echo will take less time to acquire and less time to interpret compared to the full echocardiogram. Second, we point out that the main spatiotemporal characteristics of the heart should be extracted by a computational model. Such a model will eliminate the time of the echo technician performing measurements. Expert echo reader will perform binary classification to normal and abnormal studies based on 6 views. It is estimated based on literature that 16% of studies will be classified as abnormal and will need to be followed by a full diagnostic echocardiogram [37]. We believe that the current knowledge of how the human visual system works is at the point that one can emulate perception of a naïve observer. The next step, is to enhance the model so that it can emulate the percept of an expert. The method that we propose, namely, the use of the ground truth in the form of contours and measurements, combined with tools such as shortest path in the complex-log representation may lead to dramatic improvement of the model's performance.

Once the elaborated computational model exists, one can speculate about developing a computational tool that will be guiding a relatively naïve echo user in acquiring the necessary views. This goal may be achieved in a distant future, but we think that the field is at the point where this task should be taken seriously.

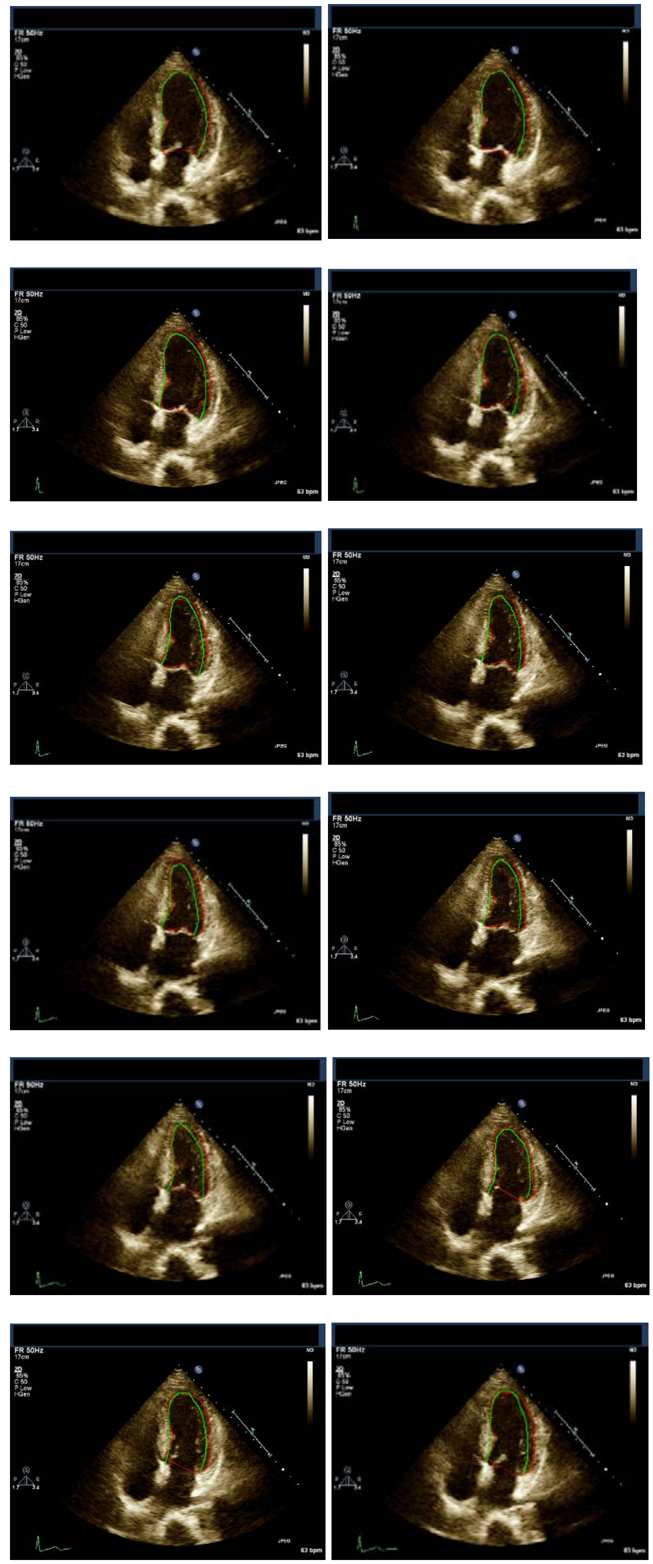

Figure 9: Every 3rd image from an echo cycle with the ground truth (green) and our model (red). The expert reader drew open contours assuming that the endpoints should be connected.

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Author Biography

Irmina Gradus-Pizlo received her medical degree from the Medical University of Warsaw, Poland, in 1984. She was a postdoctoral fellow at the NIH (1989-1991) and then at Indiana University Medical School (1991-1993). She completed her medical residency and fellowship at Indiana University Medical School in 1996 and 1998, respectively. She was an Assistant and Associate Professor of Medicine at IU Medical School (1999-2017). She is now a professor at the Medical School of UC Irvine, CA.

Kunal Agrawal is a full stack Software Engineer at Quantifi, a High Alpha portfolio company, that specializes in social media advertising research and development. He graduated from Purdue University in 2016 with a bachelor's degree in Computer Science.

Edward J. Delp was born in Cincinnati, Ohio. He is currently The Charles William Harrison Distinguished Professor of Electrical and Computer Engineering and Professor of Biomedical Engineering at Purdue University. His research interests include image and video processing, image analysis, computer vision, image and video compression, multimedia security, medical imaging, multimedia systems, communication and information theory. Dr. Delp is a Life Fellow of the IEEE, a Fellow of the SPIE, a Fellow of IS&T, and a Fellow of the American Institute of Medical and Biological Engineering.

Zygmunt Pizlo received his MSc and PhD degrees in electronics in 1978 and 1982, respectively, in Warsaw, Poland. He received his PhD degree in psychology in 1991 from the University of Maryland, College Park, MD. He is a Professor of Cognitive Sciences and Falmagne Endowed Chair in Mathematical Psychology at UC Irvine. His research interests focus on computational modeling of how the human visual system solves ill-posed inverse problems.