Leonardo da Vinci’s flights of the mind must continue: cardiac architecture and the fundamental relation of form and function revisited

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Received 17 February 2006; accepted 2 March 2006

Summary

This overview addresses the remarkable efficiency of the mammalian heart as a pump of unique capacity to quickly vary output and ejection velocity and its relation to ventricular geometry, fiber architecture, integrity of collagen scaffold and microvasculature and appropriate electrical activation. The unique functional capacity of the ventricle depends critically on the organization of cardiac muscle fibers in layers of counter-wound helices encircling the ventricular cavity in a pattern that allows a special twisting motion during systole and early diastole, essential to the mechanical efficiency of the normal ventricle to eject and suction venous return. The important contribution of advances in imaging techniques is reviewed, especially magnetic resonance with tagging and tensor analysis to define fiber orientation; these measurements are made without the use of implanted devices that can distort structure and even impair function. The impact of loss of optimal fiber orientation and geometry of the ventricle as a result of diseases that cause heart failure is analyzed, along with the possibility of improvement by carefully planned surgical restoration of ventricular geometry. The very encouraging results yielded by these therapeutic strategies are critically dependent on a clear understanding of the relation of structure and function that our analysis attempts to promote. Simultaneously, there is full acknowledgment of the unanswered questions that are inevitable but equally essential to the continuing search that scientific progress depends on.

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Keywords: Magnetic resonance imaging; Ventricular geometry; Helical ventricular myocardial band; Collagen weave; Electrophysiology; Ventricular restoration

Five centuries have elapsed since Leonardo da Vinci studied and produced masterful drawings of the cardiac valves that are inspiring new approaches to human valve reconstruction by surgeons such as Mr Francis Wells at Papworth Hospital, Cambridge, UK. His remarkably inquisitive mind led him to construct a glass blown model of the aortic outflow in which he demonstrated, by introducing small opaque seeds in the fluid he propelled through the simulated aortic valve beyond the replica of the aortic sinuses, the vortical flow of eddie currents that he depicted as the first clear experimental demonstration of the fundamental relation of form and function in the cardiovascular system [1,2].

A renewed awareness of the fact that cardiac structure conditions function, led to a fundamental workshop organized by Professor Peter Paul Lunkenheimer, held in Denia, Spain, by the European Society of Cardiology, under the patronage of the Spanish Society of Cardiology, 9—12 June 1995. Our group of more than 50 scientists included morphologists, cardiologists, physiologists, experimental cardiologists, bioengineers, and mathematicians from The Netherlands and Britain to New Zealand and from the US to Russia (Soviet Union at the time). The ensuing decade has witnessed a growing awareness of the vital importance of ventricular shape and function that has prompted the publication of an entire volume of Thoracic and Cardiovascular Surgery, Volume 13, No. 4, October 2001 on Ventricular Shape and Function in Health and Disease, with Dr Gerald Buckberg as guest editor, and caused the National Heart, Lung, and Blood Institute to convene a special workshop entitled ’Form and Function: New Views on Development, Diseases and Therapies for the Heart’ on 25—26 April 2002, in Bethesda, Maryland [3]. The results of applying fundamental concepts derived from our research on ventricular architecture and function in 1198 patients with severe congestive heart failure resulting from anterior myocardial infarction, treated by surgical ventricular restoration have recently been published [4].

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There has been a remarkable growth in the understanding of cellular myocardial function at the molecular/genetic level and even the development of the ability to perform genetic manipulation of cardiac and other cells within the heart. It remains critically important to recognize that the complex molecular machinery that enables the heart to fulfill its role in the circulatory system can only function effectively within an architectural design that allows the contractile apparatus to perform with optimal mechanical efficiency, determined by appropriate integration of the vectors of force generated by cardiac sarcomeres. This requires appropriate spatial distribution of myocytes in an optimal fibrillar structure, supported and secured by the necessary healthy collagen scaffolding and intercellular matrix, with adequate coronary perfusion and optimal electrical synchronization.

Thus, a clear understanding has evolved that anisotropy is a key feature of the myocardium, which requires that earlier models designed to explain hemodynamics and ventricular function be replaced by far more elaborate mathematical constructs [5,6] fortunately aided by the remarkable advances in cardiac imaging techniques. The understandable admiration and fascination for such models must not lead us to forget the admonition of Schmid, Niederer, Lunkenheimer and the late Torrent-Guasp that ‘an efficient ejection of blood is only reached when the myocardial weave alignment obeys some mechanically meaningful pattern’ [7] and our demonstration that the cardiac architecture of the healthy heart is Gothic (elliptical), while that of the sick heart is Romanesque (spherical), based on meticulous assessment of the curvatures of the ventricular wall from cardiac MRI in patients [8].

The NHLBI workshop of 2002 concluded that in order to confront the very serious public health problem of heart failure and develop more successful therapeutic strategies for medical and surgical therapy, a shift from the emphasis on concepts of ventricular function that consider predominantly contractile state and load to those that also incorporate interaction and dynamic rearrangement of myocardial layers is needed [4,9,10]. There have been several very comprehensive reviews of ventricular function that have covered the more classical aspects of ventricular physiology [11—14]. We will focus more intensely on anatomic concepts and models of the myocardium and how they relate to ventricular physiology and influence medical and surgical therapeutic strategies.

Torrent-Guasp proposed a challenging and very important anatomic concept in which both ventricles are considered to consist of a single myocardial band extending from the right ventricular muscle just below the pulmonary artery to the left ventricular muscle where it attaches to the aorta, twisted and wrapped into a double helical coil during evolution and embryological development, capable of highly efficient sequential contraction responsible for ventricular ejection and filling [15—19]. His anatomical ‘model’ (Fig. 1) has been misinterpreted as suggesting that the ventricular walls are composed of strap-like muscles [5]. The embryologic origin of the fundamental twist or change of direction of the fibers in the transition from what Torrent-Guasp describes as the basal portion or loop of the myocardial band and the apical loop that defines the ventricular helix has been suggested by Buckberg [20]. Important proof that the helical arrangement of fibers is not random was provided by the observation of Professor Lunkenheimer and associates who documented that, in a dog that they studied with situs inversus, the helical arrangement showed a directional inversion. Furthermore, ‘systematic force mapping with needle force probes on the beating heart in situ, affirmed a coiling of the fibers in the opposite direction. The otherwise perfectly working heart yielded a normal pattern of wall forces, yet with an inverted direction of force trajectories’ [7].

Prior to the monumental work of Hunter et al. [6] at the Bioengineering Institute of the University of Auckland, New Zealand, computational models of the heart were based on the concept that ventricular myocardium was a continuum in which myocyte orientation varied smoothly across the ventricular wall from subepicardium to subendocardium. This view assumed that ventricular myocytes were uniformly coupled to form a syncitium with material properties that are transversally isotropic with respect to the local muscle fiber axis [21—24]. The Auckland heart model [5,6] represents the most elaborate and fundamental computer modeling based on their very exhaustive investigation of fiber orientation in the heart by painstaking and novel techniques. This model is firmly based on the view that the ventricular myocardium is a morphologically and electrically anisotropic three-dimensional hierarchy of interconnecting muscle layers, separated by cleavage planes and coupled via an extensive and fundamental extracellular connective tissue network.

A mathematical representation of ventricular geometry and muscle fiber organization using three-dimensional finite elements referred to a prolate spheroid coordinate system was developed for quantitative analysis of many aspects of cardiac function [32].

The presence and orientation of myocardial fibers has been studied by anatomists over the centuries (Lower R; Senac JB; Ludwig C; Pettigrew J; Mall FP; Keith A; Robb JS and Robb RC; and Anderson RH and Becker AE) as summarized in Ref [33]. Detailed observations of ventricular myocyte orientation derived from the study of myocardial samples from limited sites, mostly with standard histological techniques in diverse species, have been reported [23—31]. These studies did not attempt to integrate their findings into models designed to analyze and explain ventricular mechanics and function like those of the Auckland investigators [6] and other authors [32—36]. Waldman et al. [37] measured transmural deformation and local myofiber direction in the anterior free wall of open chest dogs by imaging multiple columns of implanted radio-opaque beads with high-speed biplane cineradiography. Ingels et al. [34] studied the longitudinal, circumferential and oblique shortening and torsional deformation in the left ventricle of the transplanted human heart by radiography of surgically implanted markers.

These in vivo analyses represented a fundamental advance in the study of cardiac myofiber orientation and function. However, methods that depend on implantation of beads or devices into the left ventricular wall cannot sample multiple sites, could possibly interfere with myocardial deformation and can only be applied to a limited number of subjects under very special circumstances. Magnetic resonance imaging combined with MRI tissue tagging by
selective radiofrequency saturation provides a unique nondestructive means of studying three-dimensional wall motion, deformation and strain in normal and diseased hearts [38–47].

The mammalian ventricle is a highly efficient pump, providing a variable output of 5–25 l/min with a unique capacity to quickly vary output and velocity of ejection to meet changing needs. The myocardial fiber organization is central to the functional design and remarkable efficiency and adaptability of the heart in health and disease. Few would debate that cardiac muscle fibers are arranged in layers of counter-wound helices encircling the ventricular cavity which confer a special twisting motion during systole and early diastole essential for its mechanically efficient function [33,35,47]. Several lines of evidence suggest that the fiber configuration serves to equalize stresses and strains across the thick walled ventricle, allowing both active and passive (collagen scaffold and vessels) tissue components to operate in optimal mechanical regimes [35,37,48,49]. Ingels emphasized the importance of the ‘opposing force couples’ from subendocardial fibers disposed in a right handed helix and subepicardial fibers in a left handed helix (Fig. 2). The summation of these force couples is responsible for the very important torsional deformation of the left ventricle about its long axis.

The crucial role of the helical design in the heart and other biological structures has been very well described by Buckberg [50]. In fact, it has been established that during

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**Fig. 1.** 'Unfolding' of the myocardial band according to Torrent-Guasp (A–D) [94]; (E) the sequential segments of the basal and apical loops of the fully extended band.
ontogenesis, the compact layer of myocardium is initially only a few cells thick, but gradually develops a multilayered spiral architecture, linked to the continued looping in the development of the mammalian heart, as there is little evidence of spiraling in the trabeculated hearts of lower vertebrates [51]. The genes involved in the key phases of myocardial morphogenesis have been identified and mutant mice have been recognized with perturbed myoarchitecture due to disruption of certain genes, which is associated with severely compromised heart function.

The fiber angle was shown to be critical by Sallin [52] and re-emphasized by Ingels [35] and by Shapiro and Rademakers [47]. Sarcomere shortening generally does not exceed 15% [53]. For simplicity, he assumed a cylindrical ventricular model and showed that this degree of shortening could only reduce volume by 15% if fibers were disposed longitudinally, by 30% with circumferential fibers and by 60% or more with fibers oriented in an oblique spiral direction. Structural engineers who construct cylindrical containers for fluids for industrial purposes out of plastic fiber have shown us that the fibers of the wall must be placed at a 56—60° angle in crisscrossed manner to achieve maximum strength of the walls to withstand internal pressure by a well-defined mathematical formula. They asserted that in order to obtain similar wall resistance with circumferential fibers (easier to apply), the walls would have to be three times as thick.

Thus, the design of the left ventricle that has to counter internal pressure of the blood and generate the opposing pressure to efficiently eject the blood is truly remarkable. These angles correspond precisely to those proposed by Torrent-Guasp and co-workers [33] in his helical model of the myocardial architecture (Fig. 3) and to those calculated in magnetic resonance fiber strain analysis by Rademakers et al. [41] of −68% (tilted rightward from longitudinal axis) for epicardium and 74% for endocardium (leftward from longitudinal axis). Diffusion-sensitive MRI imaging in which water diffusion anisotropy proven to faithfully parallel histologic anisotropy, has been performed in three human volunteers to define the fiber orientation by eigenvector of diffusion in the normal heart non-invasively in vivo [46]. This has been
compared with the fiber orientation in cardiac necropsy specimens by the same technique (Fig. 4). The endocardial to epicardial variation of fiber helix angles is shown in Fig. 1 and presented in comparison with Streeter’s classic micrograph of transmural variation of fiber angle in the canine left ventricle, and displayed in relation to depth in the ventricular wall.

The fiber orientation coincides nicely with the plotted average angles of Streeter et al.’s [23] samples from the longitudinal section of the T distribution that he reported. The significant subsets of horizontal mid-wall fibers were found in the samples taken from the upper horizontal limb of the T. This is important, because objections to Torrent-Guasp’s myocardial band have often been based on the fact

Fig. 4. Comparison of myocardial fiber orientation studied by special histologic MRI diffusion methods: (a) fiber orientation determined by histologic methods by Streeter et al. [23] in canine ventricles; (b) helix angle of fibers defined by diffusion NMR imaging by Reese et al. [46] in human cadaveric heart, fresh cardiac necropsy specimens.

Fig. 5. Systolic ‘wringing motion’ of the human left ventricle with end systolic tagged acquisitions overlaid with ejection trajectories shown by Stuber [44].
that his descending and ascending loops of the apical portion of the myocardial band did not include a significant group of horizontal mid-wall fibers. This fiber distribution would indeed correspond to Torrent-Guasp's horizontal basal loop.

Left ventricular twist or torsion (twist per unit length) plays such an important role in efficient ejection and filling that quantitation by tagged MRI has been proposed as a reliable index of ventricular function [42] and studied with special tagged MRI in patients with diastolic heart failure [43] and pressure overload (Fig. 5) due to aortic stenosis [44] and carefully measured during the systolic and diastolic phases of the cardiac cycle [47] as well as the opposite twist which the authors described as the 'recoil of torsion' in the period of isovolumic relaxation (Fig. 6; [47]). Ingels analyzed the vital role of the collagen matrix scaffold, so well studied and described by Caulfield and co-workers [55—61] to maintain optimal stress distribution in the ventricular wall [36,48,49] while allowing some controlled fiber shear during systole and the likely 'storage' of elastic energy within the collagen struts to aid in elastic recoil during isovolumic relaxation and filling (Fig. 7).

The macroscopic myocardial band separated by gentle blunt dissection in over 1000 hearts by Torrent-Guasp has not pretended to ascertain the precise topography of individual muscle bundles within the band. The precise characterization will almost certainly be provided in vivo by advances in imaging methods such as high field magnetic resonance imaging [6] and diffusion tensor imaging, tissue tagging and strain assessment in three-dimensional space [62,63]. Buckberg et al. [33] have suggested an organizational pattern of coils within coils in the myocardial helix (Fig. 8) and presented data in support of the sequential but integrated contraction of the 'segments' of the band described by Torrent-Guasp.

There are diverse hypotheses of the spread of the electrical activation within the ventricular wall, some that propose radial conduction through sheets of muscle fibers interconnected by fiber branches and others that postulate conduction via the anisotropic conducting matrix [64] in a veritable electric spiral of the heart. The relation between structure and electrical activation is being studied with the development of a novel fiber-optic probe to record transmembrane potentials at multiple intramural sites of the intact heart in pigs [65]. Taccardi et al. [66] studied potential distribution maps of excitation and recovery obtained by extensive multi-electrode recordings in dogs at 1 ms intervals and showed that the electrical wave fronts

Fig. 6. Recoil of ventricular torsion shown by Rademakers et al. [84] using tagged MRI studies in canine hearts to define the time course and circumferential change during recoil of the canine heart.

Fig. 7. Three-dimensional arrangement of endomysial collagen fibers in left ventricular free wall [56].
followed the complex intramural pathways of myocardial fibers in a coil-like manner wound around a series of toroidal cores. More recent studies in the mouse heart have revealed a similar helical twisting of the potential wave front and shown profound alteration of activation patterns in transgenic mice with reduced expression of connexin 43 of gap junctions or a mutation of α5 integrin [67].

The helical pathway of the electrical activation is not the direct evidence for the above-mentioned coil pattern of myocardial fibers but it raises a challenging question. A three-dimensional image of the arrangement of endomysial collagen studied by special scanning electron microscopy after sodium hydroxide maceration in non-contracted rabbit heart (free wall of the left ventricle) was published in Images in Cardiology, Heart 2001 [68]. This method of maceration allowed the isolation of collagen fibers, the elimination of all other tissue elements, and the preservation of endomysial structure and position. The authors concluded that the peculiar three-dimensional architecture shown in the image ensured protection against myocyte overstretch and could provide one of the morphologic bases of cardiac muscular compliance. The disposition of the myocyte lacunae suggests a spiral disposition rather than planar 'sheets' of myocytes (Fig. 9; [68]).

The relationship between myocardial band contraction and phases of the cardiac cycle has been outlined in detail [33] and recently reviewed by Torrent-Guasp before his untimely and sad death [69]. Some very important recent studies of the embryologic development of the cardiac muscular tube and its twisting and differential growth have enhanced our understanding of how a muscular structure with an abrupt twist between the initial portion ('basal loop') and the continuation that forms the ventricular helix ('apical loop') can develop. Lunkenheimer et al. [81,82] have proposed a different model based on microergometry assessment of wall stresses with a needle device inserted into the ventricular wall of dogs and pigs, which led to the concept of a contracting mesh of fibers. They did caution that the 'measured signal maximum is not necessarily obtained when the probe's window is aligned exactly parallel to the...
histologically visualized length striation of the local fiber alignment'.

We will necessarily analyze the relation of ventricular form and function based on our personal research data and the very important information from advanced MRI studies and, in many cases, personal contact with the researchers. Contraction proceeds during isovolumetric systole rapidly from the right to the left segment of the basal loop [70-73]. The right band is activated very early corresponding to the first point of break-through of electrical epicardial potentials overlying the point of termination of the thick undivided right bundle and traversing the thin right ventricle very rapidly [74]. The sequential contraction has been assessed by meticulous placement of sonomicrometer crystals on different segments of the band [33] and correlation of their signals with the electrocardiogram and simultaneously recorded left ventricular pressure. These devices can monitor timing and duration of shortening or lengthening of the explored segment with great precision. They are not suited to investigate motion in planes outside of the segment of placement. Such orthogonal strains of fibers have been evaluated by very complex sets of radio-opaque markers studied with biplane cine-radiography [37] and are not the object of these studies and have been replaced by advanced MRI methods. A valid precaution was raised by Dr Julien Hoffman regarding accuracy of the crystal studies in late systole, as Noble [75] had shown that active contraction of the left ventricle occupied only the first half of systole by timed aortic occlusion studies in the dog. However, the author himself acknowledged in the discussion of his paper, that the ventricle was exerting considerable force in the wall during the late part of the ejection systole based on earlier work of Hefner et al. [76].

The contraction of the basal loop provides a 'fulcrum' for the apical loop and narrows the annuli of the mitral and tricuspid valves [77,78]. The mechanically very effective tightening and shortening of the descending helix in left ventricles with normal geometry and architecture displaces the base of the ventricle in an apical direction as documented by Karwatowski et al. [45], by a combination of anatomical magnetic resonance with magnetic resonance velocity mapping of left ventricular long axis and produces the counter-clockwise twist of the left ventricle demonstrated by tagged MRI [42-44,47]. This pattern of contraction produces the rapid ejection at the required pressure to overcome the impedance of the left ventricular outflow so characteristic of the healthy left ventricle. The mechanical efficiency is such that it allows the minuscule ventricular mass of a new-born with tight aortic stenosis to generate ventricular pressures in excess of 200 mmHg and survive to receive surgical therapy.

The even more Gothic architecture of the giraffe (Fig. 10; [8]) allows the ventricle to generate systolic pressures of 300 mmHg to provide cerebral perfusion with its head erect [8]. This functional advantage is lost in varying degrees by the diseased heart that does not retain the Gothic architecture and dilates to acquire a progressively Romanesque (spherical) architecture, with loss of the optimal myocardial fiber direction for efficient helical contraction (Fig. 11), and adequate distribution of wall stress [35,36,47,49,52,54]. The sonomicrometer tracings show that contraction begins at the same time in the right segment of the basal loop and the descending segment of the apical loop as would be expected from the very early arrival of the activation at the

Fig. 10. Comparison of the shape (architecture) of the amphibian, human and giraffe left ventricle. Amphibian LV represents Romanesque (circular) architecture of dilated failing heart, contrasted with the Gothic (elliptical) healthy human LV and the ‘extreme Gothic’ giraffe LV capable of generating systolic pressures of 300 mmHg routinely [8].

Fig. 11. Comparison of the normal and dilated heart, whereby the architectural patterns of the apical loop change from an oblique orientation to a more transverse pattern and begin to resemble the horizontal basal loop configuration [8].
left bundle of the Purkinje system in the upper septum. The signal of the left basal segment reveals a 10 ms delay suggesting that activation has traveled via the myocardial band itself activated early by the mechanism explained above (electrophysiological recordings show that the conduction system does not activate the basal portion of the left ventricle early). This timing does not concur with Torrent-Guasp et al.'s [69] most recent timing of the phases of the cardiac cycle. The sequence of shortening continues in the descending segment during isovolumetric systole. At the time of the peak of left ventricular positive dp/dt, left ventricular ejection begins and the shortening signal of the ascending segment begins (80 ms into the cardiac cycle). During the rapid ejection phase there is 'co-contraction' of descending and ascending segment fibers at the time that tagged MRI reveals the counter-clockwise rotation of the apex in keeping with the model of opposing force couples depicted by Ingels (Fig. 2).

It is very interesting that data obtained by suturing a Walton-Brodie strain gauge arch aligned carefully with the direction of the fibers of the anterior wall of the dog left ventricle (free wall away from left anterior descending coronary artery published by Reeves et al. [83]), revealed force generation by the myocardial fibers corresponding to the ascending loop monitored by sonomicrometry with the exact same timing. The instrumentation in the 10 open chest dogs provided simultaneous high fidelity left ventricular pressure, LV dp/dt, force exerted by the free wall fibers on the strain gauge arch, a signal from a LV circumference gauge and a surface ECG, recorded on Electronics for Medicine at 100 mm/s (Fig. 12). Tension began to rise at onset of LV ejection, coinciding with peak/positive dp/dt, reached a peak at end of ejection and declined gradually, remaining positive (force generation), throughout the period designated as isovolumic relaxation. Cessation of active contraction and elastic recoil would have been expected to produce a sudden release of the tension signal as the strain gauge would immediately return to baseline position if not opposed by active force.

We did not report this because we feared it was an artifact as the signal remained so positive ‘during relaxation’. We carefully verified the perfectly stable baseline of our gauge in spite of varying end diastolic filling, administering catecholamines and depressing contractile function with methoxamine. The continued shortening of the fibers corresponding to the ascending segment during the period designated isovolumic relaxation is fully supported by the sonomicrometer data. Shortening ends in the tracings depicting signals from the descending segment and posterior wall, but continues for 90 ms in the ascending loop tracing until the decline of left ventricular pressure is completed.

This data support Torrent-Guasp et al.'s [69] recent publication and concept of a ‘systolic’ phenomenon that plays a key role in ventricular filling even before the opening

![Fig. 12. Correlation of left ventricular pressure and fiber tension (strain gauge arch) in anterolateral left ventricular wall. Note tension coincides with peak dp/dt at end of ejection and remains positive (force generation) during the isovolumic relaxation period. An elastic recoil would be expected to cause sudden release of tension signal and immediate return to baseline.](image-url)
of the mitral valve as a result of the decline of LV pressure below that of the left atrium, a truly old debate as his publication describes. The lengthening of the ventricle after aortic valve closure and before opening of the mitral valve during which sonomicrometry suggests an initial phase of co-contraction of descending and ascending fibers of reciprocal oblique orientation, followed by relaxation of descending and continued shortening of ascending fibers, is postulated to contribute very importantly to the rapid early filling of the left ventricle. The elongation of the long axis of the LV with consequent upward displacement of the mitral valve plane has been well demonstrated by special MRI techniques (velocity mapping) and correlated with the onset of mitral diastolic flow by echocardiography and by magnetic resonance velocity mapping of mitral flow [45,85].

The diastolic velocity signal of the plane immediately below the valve preceded the flow across the mitral valve by a mean of 46 ms. Torrent-Guasp et al. [69] have presented an extensive review of the systolic contribution to ventricular filling in their recent publication and emphasized that the downward displacement of the ventricular base and ventricular torsion documented by MRI during ejection as the descending fibers shorten, changes the length and curvature of the ascending fibers before they initiate the co-contraction, creating a biomechanics that facilitates 'ventricular elongation'. They also emphasized that the very marked changes in rapid filling velocity with exercise strongly suggest an important effect of catecholamines on muscle function, as changes in the 'collagen spring loading or in titin stretching' to significantly alter restoring forces or elastic recoil would be very unlikely to develop so rapidly.

MRI has been particularly helpful in studying twisting and untwisting of the left ventricle, changes in long axis (displacement of mitral valve plane) and volume or circumference change during the phases of the cardiac cycle. A study of ventricular torsion and untwisting in the canine left ventricle showed that 50% of the untwisting occurred during 'isovolumic relaxation' before filling and before any change in circumference and led the authors to maintain that 'suction could develop'. This increased to 60% with dobutamine [84]. Prior to our demonstration of specific directional active myocardial contraction during the untwisting and change of shape of the left ventricle, this had been attributed to release of energy stored mostly in the collagen scaffold and in titin in the sarcomeres as a result of systolic deformation and described as elastic recoil.

Gillebert et al. [86] have published the most comprehensive review of ventricular relaxation and discussed the

![Fig. 13. Computer-generated images of left ventricular wall curvatures [8]. Diastolic (A) and systolic (B) images of LV wall curvatures generated by computer analysis of cine MRI (Coghlan-Singleton method), before transplantation of CHF (LV EF 15%) in left images and after transplantation (right images) as LV EF rose to 44% images.](image-url)
research on the effects of load and non-uniformity on myocardial relaxation and analyzed the timing and rate of left ventricular pressure fall in terms of cross-bridge mechanics. They have stated that 'a distinction between relaxation and diastole would introduce a subdivision which has a questionable clinical meaning'. The extensive experimental data they reviewed support an important role of myocardial fibers and their regulation in the rate and timing of left ventricular pressure decline often attributed primarily to elastic recoil. This would have important implications in possible pharmacologic treatment of diastolic dysfunction. Diastolic dysfunction has been extensively reviewed in the past decade [87—89].

Disease can profoundly alter both the function of myocytes, the collagen scaffold and the microcirculation and very importantly, the ventricular geometry, architecture and fiber orientation, with profound consequences for ventricular function that have made heart failure such a major health problem. Developments in imaging methods that make it possible to detect and quantify the functional impact of such changes of form manifested in alterations of volume assessed in three dimensional curvatures of ventricular walls (Fig. 13), ventricular torsion [42—44] and even fiber architecture by MRI diffusion study [46] have created the impetus for development of surgical techniques of ventricular modification and reconstruction [3,9,90—94].

As the diseased heart dilates acquiring the Romanesque rather than the Gothic architecture [5], fibers become more horizontal, losing the vital mechanical advantage conferred by obliquity [9,35,52]. The critical importance of improving ventricular geometry to try to regain effective fiber orientation has made the results of ventricular restoration operations (Fig. 14; [9,90]) far better than those of techniques aimed at merely reducing wall stress (Laplace’s law) by reduction of ventricular radius of the more spherical diseased heart [91]. The same principle applies to techniques designed to restrain ventricular dilatation with the purpose of limiting wall stress by a surgically placed inner buttress (myosplint) with poor results versus those of placement of an external ventricular remodeling and constraining mesh that makes the diseased ventricle more conical, thus changing fiber orientation and allowing even for progressive functional improvement due to changes in neuro-endocrine, cytokine, oxidative radical and metalloproteinase regulation [93].

The importance of ventricular geometry is being further emphasized by the three-dimensional study of blood flow patterns in the human heart by three-dimensional magnetic resonance velocity mapping in the right and left atrium, ventricle and aorta which have defined streamline pathways of blood flow in the left atrium as a vortex of counterclockwise rotation (viewed from the front) that directs flow to the mitral valve. Early diastolic inflow creates a large counterclockwise anterior vortex in the left ventricle that tends to direct flow toward the outflow tract [95—98]. Such vortical flow would have a beneficial effect of energy conservation and provide a fluidic functional advantage which would enhance the efficiency of a helical heart. The loss of this flow pattern with the geometrical and architectural changes resulting from disease induced ventricular dilatation (Fig. 15) further emphasizes the need to try to restore geometry, with its important advantages in flow dynamics that contribute to optimal ventricular function.

Fig. 14. Changes in ventricular shape after left ventricular restoration. The elliptical normal form (a) becomes spherical after anterior septal infarction (b). Size and shape are rebuilt to an elliptical configuration (c) by placing a patch into the left ventricle to exclude the scar, reduce volume and reconstruct the normal elliptical chamber [9,90].
The relatively coherent swirling of blood that results from the embryologic looping and non-planar asymmetries of the vertebrate heart [51,79,80], although potentially associated with higher wall shear stresses, might avoid excessive dissipation of energy by limiting flow separation and instability. These intracardiac fluid forces could play an important role as an essential epigenetic factor for embryonic cardiogenesis leading to the development of the helical orientation of ventricular myofibers [99]. This data on flow patterns add a further dimension to our analysis of the medical relevance of pathologies or interventions that entail altered relations between form, flow, mobility and timing in the heart and point to the fundamental of cardiac surgery to conserve or reinstate the spatial relations and mobility of cardiovascular tissues if technically possible.

Even though there may still be some controversy on the concept of the myocardial band introduced by the late Torrent-Guasp it is our hope that we may keep an open mind that allows what Dr Tinsley R. Harrison defined as ‘pre-search’, and enables us to follow Einstein’s advice that ‘the important thing is to never stop asking questions’, while always keeping in mind the admonition of the mathematician scientist Karl Popper that ‘when we do research, we never apprehend the truth, we merely reduce the level of our error’ [100].

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