

Chapter 2

The Teleost Heart: A Morphological Approach*

José M. Icardo

Introduction

Numerous review articles have reported on the morphology and physiology of the fish heart (see for instance Santer 1985; Satchell 1991; Farrell and Jones 1992; Burggren et al. 1997) through the years. The recent use of the teleost heart as an organ model has focused a lot of attention on this fish group. Genetic (see Harvey and Rosenthal 1998; Chen and Fishman 2000; Lohr and Yost 2000; Yelon 2001, and references herein) and epigenetic (Taneda et al. 2010) studies carried out in teleosts have provided deep insights into several mechanisms of great developmental significance for the heart of vertebrates. Furthermore, teleosts are being used to study several other biological mechanisms ranging from the establishment of the left–right axis (Chen et al. 1997; Nagai et al. 2010), to heart regeneration (Poss et al. 2002; Lepilina et al. 2006), to organ development in the absence of gravity (Niihori et al. 2004). Full understanding of all these data requires a thorough knowledge of the morphological aspects of the teleost heart.

The heart of modern teleosts has classically been described as being formed by four segments arranged in series: sinus venosus, atrium, ventricle, and bulbus arteriosus. Recent studies indicate that, in addition to those four chambers, all teleosts contain a conus arteriosus (Schib et al. 2002; Grimes et al. 2006; Icardo 2006) and a distinct atrioventricular segment (Icardo and Colvee 2011). Accordingly, the morphology of the heart is reviewed to include these two segments. Attention is also focused on the various structural patterns of the conus and bulbus. The architecture of the heart ventricle has been divided into four main types (Tota et al. 1983) depending on the absence, or on the presence and the extent of a compact layer.

*Contract grant number: CGL2008-04559/BOS from the “Ministerio de Educación y Ciencia,” Spain.

J.M. Icardo (✉)

Departamento de Anatomía y Biología Celular, Facultad de Medicina,
Universidad de Cantabria, c/Cardenal Herrera Oria, s/n, 39011 Santander, Spain
e-mail: icardojm@unican.es

Ventricle classifications are not merely academic. Different modes of heart performance have been attributed to the several ventricle types. For instance, completely trabeculated ventricles are thought to be unable to cope with increasing amounts of afterload. Evidence is reviewed here supporting the notion that the teleost heart can maintain high ventricular work in the absence of a compacta. In higher vertebrates, the collagenous skeleton of the heart plays an important role in myocardial mechanics (Weber 1989). However, this subject has received very little attention in the fish heart. The possible role of the heart collagenous skeleton in the maintenance of the ventricular shape and in the performance of the teleost heart is also discussed. Finally, the structure of the venous pole of the heart is reviewed. Despite the great biological importance of several species such as the zebrafish and the medaka as model organisms, this review is not focused on any particular species. Rather, it intends to reflect the enormous morphological diversity of the teleost heart, put the focus on controversial subjects, and addresses several issues of general morpho-functional significance.

The Outflow Tract: The Bulbus, the Conus, and the Conus Valves

The outflow tract (OFT) is the morphological division of the heart located between the ventricle and the beginning of the dorsal aorta. In most primitive fish, the OFT is formed by two segments: a proximal, muscular, conus arteriosus, and a distal, arterial-like, bulbus arteriosus (Icardo et al. 2002, 2005a; Durán et al. 2008; Grimes and Kirby 2009). The anatomical composition of the OFT in several other ancient fish, like hagfishes and lampreys, is unclear, but most uncertainties appear to derive from partial observations (Parsons 1930; Yamauchi 1980). In fact, the overall picture that emerges from the different studies is that the OFT of all primitive fish abides to the same general rule. Like primitive fish (Parsons 1930; Icardo 2006; Grimes and Kirby 2009), ancient teleosts show a conus and a bulbus. In all genera studied (Albula, Pterothrissus, Megalops, Elops, Tarpon), the heart shows a muscular conus arteriosus (Parsons 1930; Santer 1985; Satchell 1991). The conus is of variable length and contains up to two valve rows, with a total of four to six valves. These are the conus valves, which regulate the ventricular flow dynamics. In addition to the conus, the heart of ancient teleosts presents a distal outflow segment, the bulbus arteriosus, which opens in the ventral aorta. This segment contains connective tissue and elastic fibers (Parsons 1930). By contrast, the OFT of modern teleosts has classically been described as being formed solely by the elastic bulbus arteriosus. Consequently, the outflow valves were named bulboventricular valves.

In modern teleosts, the prominent bulbus arteriosus dominates the morphology of the heart outflow (Fig. 2.1). The bulbus is an elastic chamber with a “windkessel” function. It expands during ventricular ejection to store a large part of the cardiac stroke volume. Gradual elastic recovery allows a steady flow of blood toward the gills, preventing damage of the delicate gill vasculature (Priede 1976; Satchell 1991;

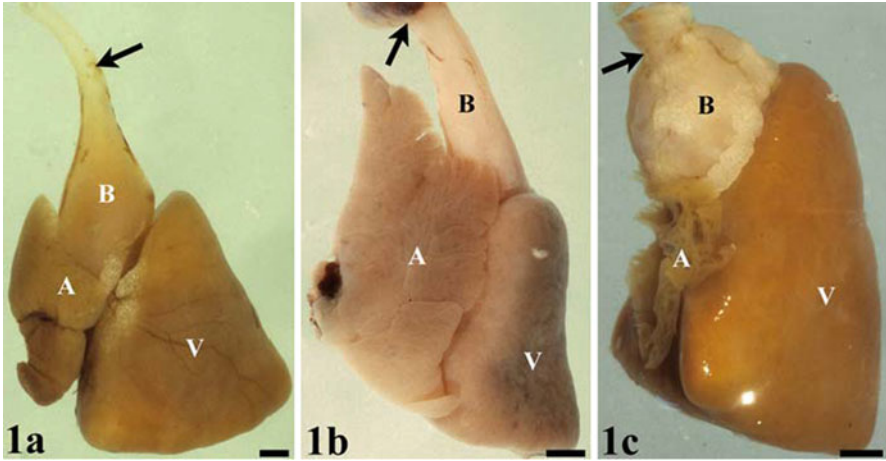


Fig. 2.1 Right lateral views of *Trachurus trachurus* (a), *Trigla lucerna* (b), and *Sparus pagrus* (c) hearts. The ventricle (V) may be pyramidal (a, c) or sac-like (b). The atrium (A) may be very large (b) or much smaller (a). The outflow tract (OFT) is dominated by the prominent bulbus arteriosus (B). No other OFT component is apparent. The bulbus is pear-shaped in (a), cylindrical and elongated in (b), and short and thick in (c). Note the relationship between the length of the bulbus and that of the ventricle: the ratio is close to a 1:1 in (a) and (b), and approximately 1:3 in (c). The arrows mark the upper insertion of the pericardium and the boundary between the bulbus and the ventral aorta. Scale bars: 0.1 cm (From Icardo 2006, Anat. Rec. A, 288:900–908)

Farrell and Jones 1992; Jones et al. 1993). To this end, the wall of the bulbus is endowed with high amounts of elastin material and an external (subepicardial) collagen layer, which probably controls bulbus compliance by limiting circumferential deformation (Icardo et al. 1999a).

From the morphological point of view, the external shape of most bulbus ranges from pear-shaped, to elongated, to thick and robust (Fig. 2.1). The wall of the bulbus is organized into layers: the endocardium, the endocardial ridges, the middle layer, the subepicardium, and the epicardium (Fig. 2.2a, b). Given the high level of radiation in fish, the existence of various shape patterns is not surprising. The surprising fact is the high variability in bulbus structure. A series of studies carried out in our laboratory (Icardo et al. 1999a, b, 2000a, b) has shown that the structure of the bulbus is close to being species-specific. The inner surface of the bulbus is characterized by the presence of ridges (Fig. 2.2a, b). These are longitudinal columns, which occupy the full length of the bulbus (Fig. 2.2a). On the whole, they are thicker at the base of the bulbus and attenuate toward the ventral aorta. Depending on the species, the ridges may be very prominent (Fig. 2.2a, b) or much more discrete (Icardo et al. 2000b). However, the real significance of these variations is currently unknown. The inner surface of the ridges is covered by endocardium (Fig. 2.2b). The ridge endocardium shows histological differences across species, ranging from squamous to columnar (Icardo et al. 2000b). In addition, endocardial cells in many species contain moderately dense bodies (Benjamin et al. 1984) of (mostly) unknown nature. The presence of the dense bodies indicates a secretory function, which may

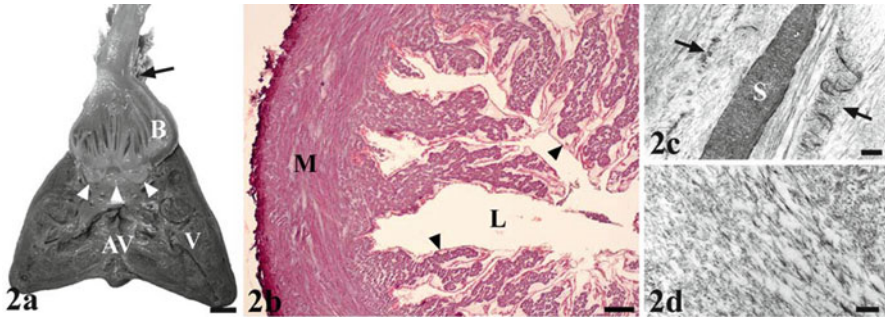


Fig. 2.2 Bulbus and conus in different teleost species. (a) *Thunnus alalunga*. Internal heart structure. The outflow tract, the ventricle (V), and the atrioventricular (AV) regions are exposed. The bulbus (B) shows well-marked longitudinal ridges. The cranial bulbus boundary corresponds to the pericardial insertion (arrow). The conus supports three semilunar valves of roughly equal size (arrowheads). The ventricle is pyramidal and appears mostly formed by a thick compacta. The AV orifice is guarded by the AV valves. (b) *Trigla lucerna*. Cross-section of the bulbus. Hematoxylin–eosin. The ridges protrude into the lumen (L) and are covered by endocardium (arrowheads). The middle layer (M) contains large amounts of extracellular material. The subepicardial layer (dark in the picture) is rich in collagen. (c) *Anguilla anguilla*. TEM micrograph of the middle layer of bulbus. A smooth muscle cell (S) is surrounded by elastin and fibrillar material interspersed with collagen fibers (arrows). (d) *Trematomus bernacchii*. TEM micrograph of the middle layer of bulbus. The extracellular matrix is formed by a filamentous network. Note the absence of collagen and elastin. Scale bars: (a) 0.5 cm; (b) 100 μ m; (c) 1 μ m; (d) 0.5 μ m; (c) from Icardo et al. 2000a, Cells Tissues Organs, 167:184–198; (d) from Icardo et al. 1999b, Anat. Rec. 256:116–126

be different between older and more modern teleost families (Leknes 2009). This secretory function appears to be enhanced in the bulbus of the Antarctic teleosts (Icardo et al. 1999a, b), where endocardial cells may be implicated in the production of anti-freeze mucins. Of note, endocardial cells in other heart chambers show scavenger functions (Seternes et al. 2002), bind natriuretic peptides (Cerra et al. 1997), are a source of endogenous nitric oxide (Imbrogno et al. 2003), or may be involved in autocrine/paracrine regulation of the subjacent tissue (for a recent review, see Icardo 2007). The middle layer of the bulbus contains smooth muscle cells and variable amounts of elastin. It may also contain, as in the common eel (Fig. 2.2c), a few collagen layers interspersed with the elastin material (Icardo et al. 2000a), or, as in tuna, collagen bundles, blood vessels and nerves (unpublished observations). However, it may lack elastin, as in the Antarctic teleosts (Icardo et al. 1999a, b). In these species, the elastin material is replaced by a fibrillar network (Fig. 2.2d), which is probably made up of glycosaminoglycans. The subepicardium is a thin layer rich in collagen and elastin, fibroblasts, vessels, and nerves (Icardo et al. 2000b). Although this constitutes a general description, the subepicardium of the bulbus can be a more complex layer. For instance, it may contain lymphocytes, plasma cells, and dendrite-like cells, and has been implied to be involved in the development of the humoral immune response (Icardo et al. 1999b). This is surprising, but it is not an isolated feature in fish. The subepicardium of the sturgeon contains thymus-like tissue (Icardo et al. 2002) which has been implicated in the

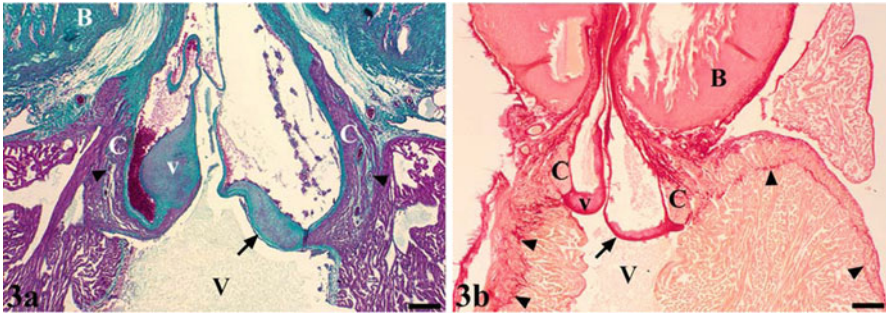


Fig. 2.3 Conus arteriosus in two hearts with different ventricular structure. B, bulbus; C, conus; V, ventricle; v, conus valves. **(a)** *Spondylosoma cantharus*. Martin's trichrome. The compact musculature of the conus differentiates easily from the completely trabeculated ventricle. Conus vessels (arrowheads) are apparent. **(b)** *Echiichthys vipera*. Sirius red. A collagenous ring isolates the conus myocardium from the ventricular myocardium. The conus valves are anchored to the conus and show a proximal stout body and a thick, luminal fibrosa (arrow). In **(b)**, a thin rim of collagen (arrowheads) locates at the boundary between the compact and spongy layers of the ventricle. Scale bars: 200 μ m

establishment and the maintenance of the cellular immune responses. The absence of elastin in stenothermal teleosts may be considered a sort of adaptation to subzero temperatures. However, the rationale for the structural variety in temperate teleosts is unknown. A number of factors such as cardiovascular dynamics, lifestyle, eco-physiology, range of diversification, may have specifically adapted the fine bulbus structure to comply with its “windkessel” function.

The conus arteriosus, present in ancient teleosts (see above), was thought to have disappeared in more derived species. The loss of the conus was attributed to intussusception into the ventricle (Smith 1918), or it was considered a direct consequence of heart evolution (Santer 1985). However, evidence raised in the last decade indicates that the conus is not lost at all in the heart of modern teleosts (Schib et al. 2002; Icardo et al. 2003; Grimes et al. 2006; Icardo 2006). Examination of up to 28 species belonging to different families and orders (Icardo 2006) has revealed that the conus arteriosus is a distinct anatomical segment interposed between the ventricle and the bulbus arteriosus. The Macrouridae (Greer Walker et al. 1985) could also be added to that list (discussed in Icardo et al. 2003). However, species differences do exist (Fig. 2.3). The conus is easily recognizable in hearts whose ventricles lack a compact layer (Fig. 2.3a), and may be more difficult to discern in hearts possessing a compacta (Fig. 2.3b). It is formed by compact myocardium (very evident in completely trabeculated ventricles), and contains more collagen, elastin, and laminin than the ventricular muscle. With very few exceptions, the conus contains vessels (Fig. 2.3a) even when the neighboring myocardium is not vascularized (Icardo 2006). As occurs with other fish hearts having conus, the teleost conus arteriosus supports the outflow valves, which should more properly be named conus valves (Schib et al. 2002).

Most teleosts possess a single row of conus valves formed of two (left and right) pocket-like leaflets and the supporting sinus (Fig. 2.3). Only a few species pertaining to the order of the Elopiformes show two valve rows (Parsons 1930). In modern

teleosts, a third valve, mostly rudimentary, may appear on the ventral or the dorsal side of the conus (Icardo et al. 2003). However, this situation does not appear to be universal. Examination of up to 40 specimens of *Thunnus alalunga* shows the constant presence of three leaflets of roughly equal size, the third one being located dorsally (Fig. 2.2a).

Each valve leaflet presents a stout proximal body, anchored to the conus, and a flap-like distal region that enters the bulbus (Fig. 2.3). The leaflets present a thick luminal fibrosa, which probably bears most of the stress generated by the backflow of blood (Icardo et al. 2003; Icardo 2006). This is a feature shared with other fish groups (Sans-Coma et al. 1995; Icardo et al. 2002), but it is opposite to the situation observed in mammals, where the fibrosa is located on the parietal side of the leaflet. Differences in extracellular matrix composition have been described in the conus valves of several teleost species (Greer Walker et al. 1985; Raso 1993; Icardo et al. 2003). These differences in composition may be implicated in the mechanical function of the valve. At least in several species (Schib et al. 2002; Icardo et al. 2003; Icardo 2006), the conus myocardium has a distinct structural organization, which has also been implicated in valve physiology.

The Ventricle

The teleost heart ventricle is a chamber that shows (Fig. 2.1) considerable species variability (Santer 1985; Farrell and Jones 1992). Indeed, this assertion can be applied to all fish heart ventricles (Santer 1985). The external shape, the architectural organization, the histology, the coronary distribution, the relative mass, the work dynamics, etc., vary widely between species. In an attempt to classify this variability, several authors have grouped the ventricles into broad categories (Greer Walker et al. 1985; Santer 1985; Tota 1989). The problem is that the ventricles do not quite fit into any particular category very often. This is especially true when data between different categories are crossed. Nonetheless, divisions based on the external shape of the ventricle (Santer 1985), or on the degree of “muscularization” and vascularization of the ventricular wall (Tota 1989), have proven useful.

The external ventricular shape has been grouped (Santer 1985) into three main categories: tubular, sac-like, and pyramidal (Fig. 2.1). This division has several functional implications. For instance, pyramidal ventricles have been related to an active lifestyle, a robust ventricular wall, and a high output work. The salmonid and scombrid families present this type of ventricle (Farrell and Jones 1992). The very active tuna also shows a pyramidal ventricle (Fig. 2.2a). However, the presence of a pyramidal ventricle does not correlate with either a robust ventricle or a very active lifestyle in many other cases such as in the Antarctic teleosts and in members of the sparid and serranid families. The significance of the two other morphologies is unclear (Farrell and Jones 1992). Furthermore, the relation between the external ventricular shape and the inner architecture is not constant (Simoes et al. 2002). Sac-like ventricles are observed in many marine teleosts, and tubular ventricles are frequently observed in fish which, like the eel, present an elongated body shape.

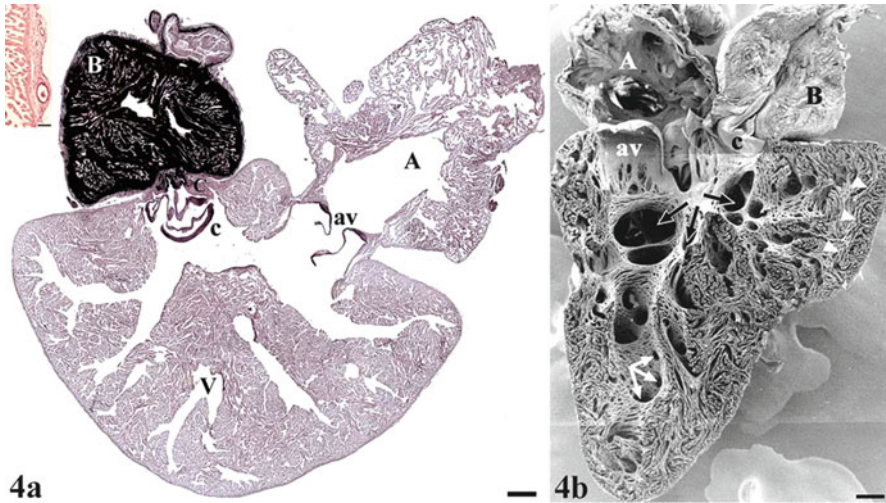


Fig. 2.4 Hearts with completely trabeculated ventricles. A, atrium; av, atrioventricular valves; B, bulbus; C, conus; c, conus valves; V, ventricle. **(a)** *Balistes carolinensis*. Orcein. The elastic bulbus is intensely stained. The ventricle is saccular and entirely trabeculated. The AV orifice is delimited by a ring of compact myocardium. The atrium shows a complex network of thin trabeculae which originates from the AV orifice. *Inset*: Detail of coronary vessels in the ventricular subepicardium. **(b)** *Sparus auratus*. SEM composite shows the architectural organization of the heart, sagittal section. The left side of the heart is shown from the right. In the ventricle, an interconnected system of trabecular sheets and lumina (black and white arrows) radiate outward from the main ventricular lumen. The lumina become smaller (white arrows) toward the periphery. At the ventricular periphery, the trabecular sheets give origin to a system of single trabeculae that reach the outer myocardial layer. Note the formation of arch systems (arrowheads). Scale bars: **(a)** 100 μ m; *inset*, 20 μ m; **(b)** 50 μ m. **(b)**, from Icardo et al. 2005b. J Exp Zool., 303A:665–675)

Another heart classification (Tota et al. 1983; Tota 1989; Tota and Garofalo 2012) relies on whether the ventricle presents a compact layer, on the relative thickness of the compacta, and on the extent of myocardial vascularization. Type-I hearts show entirely trabeculated ventricles and lack a compacta. The ventricles of the rest of the heart types present both an external compacta and an inner spongiosa. Type-II hearts show vessels in the compacta but not in the spongiosa, and type-III hearts have vessels in both the compacta and the spongiosa. Type-IV hearts are different from type-III hearts in that a large proportion of their ventricular mass is formed by a compacta.

Most teleost ventricles (close to 80%, Santer 1985) are entirely trabeculated and thus belong to type-I hearts (Fig. 2.4a). The trabecular network has been described as a highly organized system of small lumina and trabecular sheets which radiate outward from a central lumen (Fig. 2.4b) (Munshi et al. 2001; Icardo et al. 2005b). The size of the lumina decreases progressively toward the ventricular periphery. Of note, a similar pattern is observed in the spongy component of ventricles having a compacta (Pieperhoff et al. 2009). Although observations have been made in just a few species, this architectural arrangement may be more common than previously

realized. It transforms the ventricle into a multi-chambered segment formed of a small number of lumina separated by trabecular sheets. This arrangement has important functional implications. The main ventricular lumen would support the highest amount of stress, and the stress would be progressively attenuated toward the periphery. The trabecular sheets would produce enough contractile force, and the communication between the different lumina would facilitate blood squeezing (Icardo et al. 2005b).

Coronary vessels have been reported to be nearly absent in the ventricles of type-I hearts. In fact, coronary vessels are thought to be present in just a few species of temperate teleosts and to be mostly absent in stenothermal species. However, the conus arteriosus (Icardo 2006) and the atrioventricular segment (Icardo and Colvee 2011, see below) show vascular profiles in most of type-I hearts examined. More importantly, this is accompanied by the presence of vessels in the ventricular subepicardium (Fig. 2.4a, inset). Strikingly, this feature is not restricted to temperate teleosts. Coronaries are also observed in the Antarctic species *Dissostichus mawsoni* (Icardo and Colvee 2011) and *Nothotenia angustata* (Eastman 1993). Overall, ventricular subepicardial vessels are not very numerous, and they do not appear to form a very rich plexus. Consequently, their presence may have been underestimated. On the other hand, their exact role in this type of hearts is unclear. It is assumed that myocardial cells in the entirely trabeculated ventricles are supplied by the blood flowing through the ventricular chamber.

The ventricle of many other teleost species shows both a compacta and a spongiosa (Fig. 2.5), belonging to type-II hearts. The compacta is formed by myocardial cells arranged into bundle layers which appear more complex and thicker in more athletic fish (Sánchez-Quintana and Hurlé 1987; Farrell and Jones 1992). The bundles are oriented in different directions (Fig. 2.5b) forming interrelated loops and coils, which provide the structural basis for developing high blood pressures (Farrell and Jones 1992). The compact layer is always vascularized, while the spongiosa is not. However, several species do not fit well within this classification. For instance, a large part of the ventricular wall thickness in tuna is formed by a very thick, extensively vascularized compacta (Fig. 2.5b). Curiously, an apparently extensive vascular network is also observed in the spongy layer (Fig. 2.5c). Thus, the overall ventricular architecture of tuna is closer to that of type-IV hearts.

The existence of the two muscular components does not mean that all ventricles have a similar structure. The thickness of the teleost compacta may range from a mere two- to three-cell-thick layer (as in *Echiichthys vipera*) to occupy a large part of the ventricular thickness (as in tuna). Estimations of the thickness relation between the spongiosa and the compacta in type-II hearts indicate that it ranges from about 30 (as in *E. vipera*), through 10 (as in *Oncorhynchus mikiss* and *Salvelinus alpinus*), to 3 (as in *Trachurus trachurus*). It should be stressed that these values are rough estimates and have been obtained at the mid-ventricle level. The thickness of the compacta is not completely regular, undergoing variations from apex to base. Percentage values between the relative mass of the ventricle and that of the compacta have been reported earlier (Farrell and Jones 1992) for several teleost species. However, the relation between the two muscle components, albeit specific,

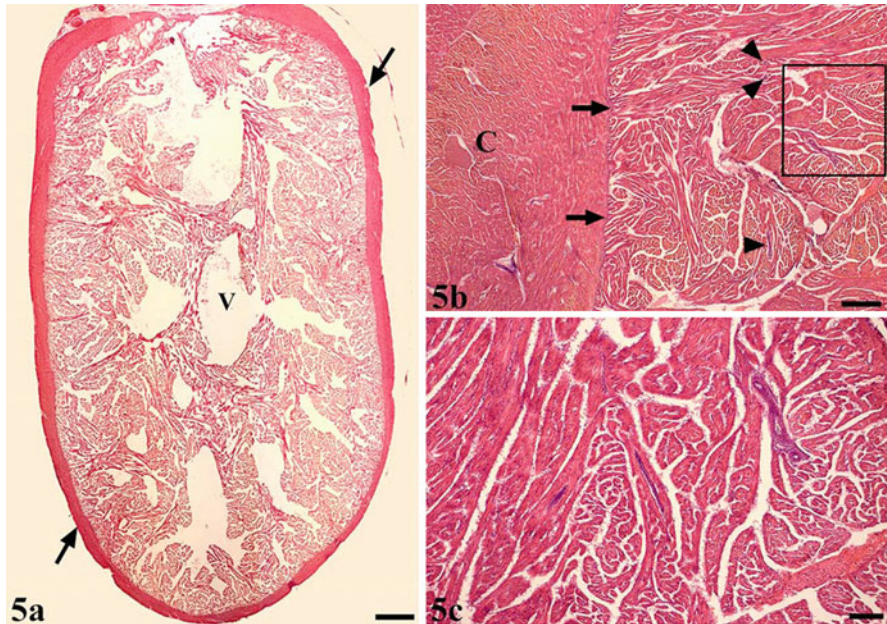


Fig. 2.5 Ventricular organization in hearts with compacta and spongiosa. (a) *Oncorhynchus mikiss*. Hematoxylin–eosin. Detail of the ventricular chamber (V). The outer compacta (arrows) limits the ventricle. Note the unequal thickness of the compacta and spongiosa. (b) *Thunnus alalunga*. Detail of the ventricular structure. The compacta (C) is organized into bundles showing different orientations. Arrows indicate the compacta–spongiosa boundary. The spongiosa shows numerous vascular profiles (arrowheads). (c) Detail of the boxed area in (a). Coronaries of different sizes are clear. Scale bars: (a) 1 mm; (b) 300 μ m; (c) 100 μ m

is not an invariable value. The proportion of the compacta has been reported to vary with changing seasons (Farrell and Jones 1992) and growth (Farrell et al. 1988; Cerra et al. 2004), but not with physical activity (Farrell et al. 1990). It should be mentioned that both the compacta and the spongiosa are formed by typical cardiomyocytes (Yamauchi 1980; Santer 1985; Cerra et al. 2004; Icardo et al. 2005b) whose structural, functional, and metabolic characteristics have been reviewed a number of times through the years (Yamauchi 1980; Santer 1985; Farrell and Jones 1992; Burggren et al. 1997). The different morphological arrangements do not depend on distinct characteristics of the myocardial cells, but on the specifics of the heart design.

Much less interest has been placed on the way the compacta and the spongiosa become structurally connected to form a functional unit. The basic problem derives from the overall circumferential arrangement of the compacta, to which the overall perpendicularly arranged spongiosa must be attached. If the two components are not connected tightly, they would tend to separate from each other. In fact, the spongiosa can be peeled off from the compacta quite easily after fixation (Farrell et al. 2007). The existence of a layer of connective tissue located at the boundary between

the two muscle components was considered to act as bonding glue (Poupa et al. 1974; Tota 1978). This concept has recently been challenged (Pieperhoff et al. 2009) in the salmonid heart, where the collagenous layer between the compacta and the spongiosa is quite discrete. It has been suggested that the outer myocardial cells of the spongiosa bend their tips to create a parallel attachment surface. This surface is enriched in desmosome and fascia adherens elements (Pieperhoff et al. 2009). The presence of a high number of intercellular junctions would create a strong attachment surface (Pieperhoff et al. 2009), providing the force necessary to maintain the compacta and the spongiosa together. However, our own observations indicate that collagen is always present, albeit in variable amounts, at the compacta–spongiosa boundary (Fig. 2.3b). Rather than rejecting any of the two alternatives, it is suggested that the combined effect of the cellular junctional elements and the extracellular matrix establish the synergy needed to sew the two muscle components together, allowing at the same time for a coordinated ventricular contraction. This is in line with the early observation that both collagen and desmosomes accumulate at the junction between the two muscle compartments (Midttun 1983).

It has also been suggested that a similar junctional arrangement could be present at the outer myocardial boundary in entirely trabeculated hearts (Pieperhoff et al. 2009). This occurs in hearts with spongy ventricles, like in the African lungfish (Icardo et al. 2005a), and may also occur in many teleosts. However, it does not appear to be a universal feature. In the teleost *Sparus auratus*, the outer myocardium forms a continuous single-cell layer, like a shell, to which the trabecular muscle cells become attached in a mostly perpendicular direction (Icardo et al. 2005b).

Another subject which has received little attention in fish is the possible role of the connective tissue in the maintenance of the architectural design of the ventricle and in the mechanical performance of the heart. The presence of a collagenous scaffold in the avian and mammalian hearts provides structural support for the myocardium and appears to play an important role in myocardial mechanics (Caulfield and Borg 1979; Weber 1989; Icardo and Colvee 1998). Collagen is an important component of the subepicardial tissue in fish. In teleosts, it may increase ventricular resilience and limit ventricle deformation (Icardo et al. 2005b). Subendocardial collagen and coiled collagen fibers running along the main trabecular axis have been described in the teleost heart ventricle (Sánchez-Quintana et al. 1995). However, the exact role of this collagen, or even the existence of a collagen scaffold, is still unclear.

A simple method to visualize the collagen network is to digest the tissue with NaOH. This preserves the collagenous component, which can then be observed with the scanning microscope (Ohtani 1987). When this procedure is applied to entirely trabeculated ventricles, the pieces of tissue are reduced to threads during processing. This indicates the absence of a collagenous scaffold which could have strong implications in either the maintenance of shape or the ventricular performance. These negative findings reinforce the role of the trabecular architecture in heart dynamics. In heart ventricles having a compacta the situation appears to be quite different. Unpublished observations in the common eel show the presence of an extensive collagen network extending between the subepicardium and the spongiosa (Fig. 2.6a). This network mimics the distribution of the muscular bundles in the compacta and the architecture of the spongiosa. Collagen connections between the

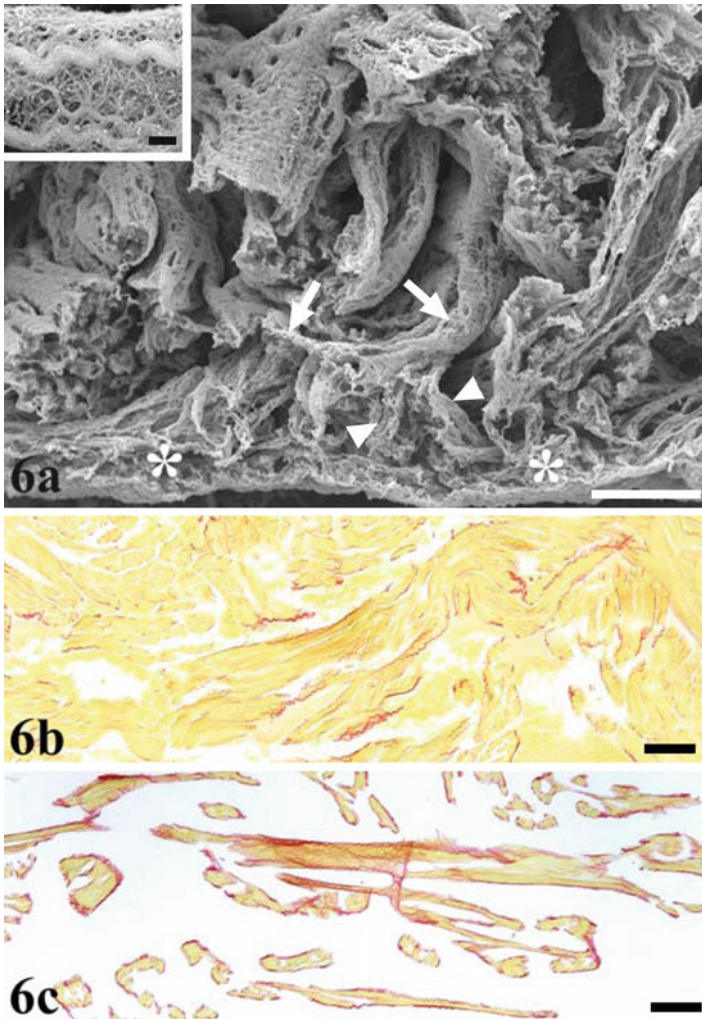


Fig. 2.6 Collagen arrangement in the ventricular chamber. (a) *Anguilla anguilla*. SEM micrograph depicting a portion of the ventricle digested with NaOH. The collagenous skeleton reproduces the ventricular architecture. Trabecular sheets (arrows) reach the compacta (asterisks). Arrowheads, arch system. *Inset*: Trabecular surface. Wavy collagen bundles run superficially and are joined by thin collagen fibrils. (b) *Anguilla anguilla*. Sirius red. Wavy collagen bundles (in red) run along the surface of the ventricular trabeculae. Collagen is nearly absent at the inner side of the trabeculae. (c) *Monopterus albus*. Sirius red. The trabecular collagen shows the same distribution as in (b), despite that the ventricle lacks a compacta. Scale bars: (a) 150 μm; *inset*, 5 μm; (b) 100 μm; (c) 100 μm

compacta and the spongiosa are numerous (Fig. 2.6a). Furthermore, collagen in the trabeculae occupies a subendocardial location (Fig. 2.6a, inset), the muscle cells occupying a central position (Fig. 2.6b). Curiously, the distribution of collagen in the trabeculae is similar in type II (Fig. 2.6b) and type I (Fig. 2.6c) hearts.

These observations are not meant to infer the existence of a common pattern for all teleost species having a compacta. However, the collagenous skeleton observed in the eel ventricle is similar to that obtained in sturgeons (Icardo et al. 1996). At least in the eel, the collagen network should play an important role in the maintenance of the ventricular architecture. In addition, its presence raises several questions of biological importance. For instance, does this network play a functional role similar to that described in the mammalian heart? The answer is unclear as yet, but the improvement of ventricular performance observed in the eel heart during growth occurs concomitantly with an increase in the amount of interstitial collagen (Cerra et al. 2004). On the other hand, the collagen connections between the compacta and the spongiosa should play an important role in the bonding of the two muscular components of the ventricle (see above).

From a functional point of view, the presence of pyramidal ventricles having a compacta has been associated with species showing active lifestyles (Santer et al. 1983). These hearts are able to sustain high levels of stroke work by pumping small volumes of blood at high heart rates against relatively high blood pressures. They work as pressure pumps, as much as the mammalian hearts do. The heart of the extremely active tuna constitutes the prototype of the pressure pump. At the opposite end of the functional spectrum (Tota et al. 1997), other hearts work as volume pumps. They are also able to maintain high levels of stroke work. However, they do it by pumping large blood volumes against low blood pressure. Cardiomegalia and bradycardia define these hearts functionally. The Antarctic teleost *Chionodraco hamatus* is the prototype of the volume pump. This species shows low activity, and its ventricle is entirely trabeculated. Curiously, it is also pyramidal. It can be argued that the morpho-functional design of the heart in the Antarctic teleosts is very specific and that it has developed as the result of adaptation to extreme climate conditions. However, it appears clear that the external shape and the inner architecture of the ventricle do not allow to establish, at least in many cases, the performance characteristics of the heart (for a comparative functional analysis between teleosts and other fish species, see Farrell and Jones 1992; Tota and Gattuso 1996, and references herein).

A related question is whether the hearts are able to sustain increasing levels of afterload. For instance, the extreme morpho-functional adaptation of the hearts of the Antarctic teleosts makes them fail when afterload is increased. This is very patent in the icefish *C. hamatus* (Tota and Gattuso 1996), and less remarkable in other Antarctic species such as *Trematomus bernacchii* (Farrell and Jones 1992). In fact, only hearts with a pyramidal ventricle and a compacta were thought to be able to cope with significant increases in afterload (Farrell and Jones 1992). A recent study has challenged this view. The teleost *S. auratus* that has a pyramidal ventricle (Fig. 2.4b) is able to increase ventricular work significantly, and to maintain cardiac output, when the output pressure is increased (Icardo et al. 2005b). This occurs without significant variations in heart rate. Thus, the heart of *S. auratus* works like a pressure pump, in a similar way as the hearts of very active species such as salmonids and tuna (Farrell and Jones 1992). The remarkable thing is that the ventricle of *S. auratus* lacks a compacta (Fig. 2.4b). It is still unknown whether other hearts with a

similar morphological pattern may perform similarly. What appears clear is that the functional capabilities of the teleost heart cannot be directly inferred from examination of the external heart shape or the myoarchitectural design.

The Atrioventricular Region

The atrioventricular (AV) region is formed by a ring of cardiac tissue which supports the AV valves (Santer and Cobb 1972; Farrell and Jones 1992). This succinct description, together with several references to the presence of a delay in the electrical conduction in the heart (Satchell 1991; Sedmera et al. 2003), sums up most of our knowledge of this part of the heart. However, recent morphological analyses show a more complex picture (Icardo and Colvee 2011). When the heart of teleosts with completely trabeculated ventricles is examined, the AV region appears formed by a distinct ring of myocardium (Fig. 2.7a, b). This myocardium is compacted, shows vascular profiles in most of the species, and contains variable amounts of collagen and elastin (Icardo and Colvee 2011). These three characteristics differentiate clearly the AV area from the ventricular and atrial chambers. A ring of connective tissue contributes to delineating the AV muscle from that of atrium and ventricle. In hearts possessing a compacta (Fig. 2.7c, d), the histological differences with the neighboring musculature are maintained, and the ring of connective tissue also contributes to differentiating the AV segment (Sedmera et al. 2003, for observations in the zebrafish). It should be stressed that the isolation of the AV muscle ring from the surrounding musculature is by no means complete. Areas of continuity with the atrial and ventricular muscle are always observed (Fig. 2.7) (Icardo and Colvee 2011). From a morphological point of view, the AV region constitutes a distinct segment of the adult teleost heart. Furthermore, the morphological appearance of the AV segment parallels that of the conus in all hearts examined (Icardo 2006; Icardo and Colvee 2011). This includes the presence of vessels.

Regarding the vascular supply of these two segments, there are several relevant features which should be mentioned since they reflect both the diversity of the teleost heart and the difficulty to establish categories of general significance. As stated above, the conus arteriosus and the AV segment show vessels in most of the species examined. However, vascular profiles could not be demonstrated in several species such as *Mullus surmuletus*, *Coris julis*, and most of the Antarctic species (Icardo 2006; Icardo and Colvee 2011). In these cases, endocardial extensions (endocardial sinusoids) penetrate the compact muscle and appear to substitute the coronary vessels. That is, the compact myocardium takes the blood supply directly from the heart lumen. In another species, *Periophthalmodon schlosseri*, the vascular endothelium present in the AV muscle is continuous with the atrial endocardium. These vascular profiles, instead of representing a true coronary circulation, may correspond to some kind of endothelial sinusoids. (The term sinusoid is applied here in a general sense. The existence of endothelial fenestrations is currently unknown.) The observations made in *P. schlosseri* cast some doubts on the real nature of the

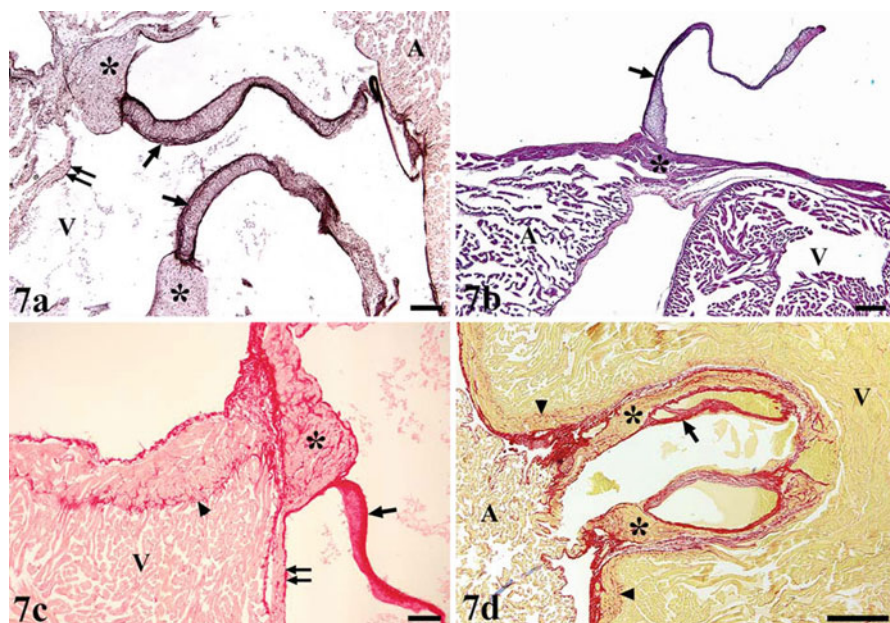


Fig. 2.7 Composite showing the atrioventricular (AV) region of type I (a, b) and type II (c, d) hearts. A, atrium. V, ventricle. In all cases, the AV valves (arrows) anchor to a ring of compact, vascularized myocardium (asterisks). The arrows also indicate the thick atrial fibrosa of the leaflets. The myocardial AV ring is partially isolated from the atrial and ventricular musculature by a layer of connective tissue rich in collagen. The collagen appears red in (c) and (d). Double arrows in (a) and (c) indicate continuity between the AV muscle and the ventricular trabeculae. Arrowheads in (c) and (d) indicate the presence of collagen at the compacta–spongiosa boundary. (a) *Serranus cabrilla*. Orcein. Note the robustness of the AV ring. The dense cellular core of the valve leaflets is apparent. (b) *Balistes carolinensis*. Hematoxylin–eosin. The AV ring is thin but the compactness of the myocardium contrasts with the delicate ventricular and atrial musculature. (c) *Echiichthys vipera*. Sirius red. The connective tissue ring separates the AV myocardium from the ventricular compacta. (d) *Anguilla anguilla*. Sirius red. The entire AV ring is exposed. Note the continuity between the AV and the atrial muscle. Scale bars: 100 μ m

myocardial vessels found both in the conus and in the AV segment in several teleosts. Yet in other cases, like in *E. vipera*, coronary vessels co-exist with endocardial sinusoids in continuity with the heart lumen. It appears that several species have developed a dual mode of blood supply for the myocardium, or that part of the vascular profiles may represent a primitive form of the mammalian Thebesian system.

Irrespective of the mode of vascular supply, the morphological evidence that the conus arteriosus and the AV region are distinct segments of the teleost heart is important from the phylogenetic point of view. Interestingly, the segmental division of the adult fish heart is similar to that found in the heart of higher vertebrates during embryogenesis (Moorman and Christoffels 2003; Wong et al. 2012). In higher vertebrates, the two heart segments exhibit specific patterns of gene expression (He and Burch 1997; Franco et al. 1999; Horsthuis et al. 2009) during development. These genetic patterns appear to be conserved across the evolutionary scale (Chang et al. 2004;

Beis et al. 2005; Rutenberg et al. 2006; Scherz et al. 2008; Shimada et al. 2009). The two segments also exhibit specific morphogenetic properties such as the induction of cushion tissue and the formation of valves (Eisenberg and Markwald 1995). Thus, despite that the conus and the AV segment are not septated in fish, they are conserved across the evolution of the vertebrate heart and appear to share many molecular and functional characteristics.

The AV valves are generally formed by two leaflets (Figs. 2.4b and 2.7) that contain numerous cells grouped into a dense core, and large amounts of connective tissue. The leaflets exhibit a strong atrial fibrosa rich in collagen (Fig. 2.7) and elastin. Within the leaflets, the cell number, the cell morphology, and the amount of extracellular material vary widely between species (Icardo and Colvee 2011). A system of chordae, similar to that observed in mammals, is always absent (also, see Hu et al. 2000). However, ventricular trabecular sheets can often be seen anchored in the AV muscle ring (Sedmera et al. 2003; Icardo and Colvee 2011). These sheets should bear some of the stress generated by the ventricular contraction and could represent a primitive form of the papillary system.

The Atrium and the Sinus Venosus

The teleost atrium is a single chamber which shows considerable variability in size and shape between species (Fig. 2.1) (Santer 1985; Farrell and Jones 1992). It is formed of an external rim of myocardium and of a complex network of thin trabeculae (pectinate muscles) (Fig. 2.4a). The presence of two arcuate systems of pectinate muscles, fanning out from the atrioventricular aperture, has been described in several teleosts (Santer 1985). The atrial myocardium is surrounded by a subepicardial, thick layer of collagen (Fig. 2.3b). Collagen also encircles the atrial trabeculae. In general, the trabecular collagen is more abundant in the atrium than in the ventricle (Figs. 2.3b and 2.7d). It probably helps to support the atrial architecture. However, the significance of this feature in terms of chamber contraction and distension is unclear.

The sinus venosus is a thin-walled chamber whose composition varies between species. It is generally described as being formed by muscle and connective tissue. However, the proportion of the two components appears to vary widely. The sinus venosus wall may be mostly made up of connective tissue (as in *Danio rerio*), of connective tissue with sparse myocardial bundles (as in *Pleuronectes platessa*), or mostly of myocardium (as in *Anguilla anguilla*) (Santer and Cobb 1972; Yamauchi 1980; Farrell and Jones 1992). To add more variation, the myocardium may be replaced by smooth muscle cells in other species such as *Cyprinus carpio* (Yamauchi 1980). The sinus venosus conveys the blood into the atrium from which it is separated by the sinus valve (Yamauchi 1980).

An important characteristic of the sinus is that it contains the heart pacemaker. In most teleosts, the presence of a specialized ring of tissue located at the sinoatrial region has been identified as the primary pacemaker region. This area is also densely

innervated (Yamauchi 1980). Other components of the cardiac conduction system, similar to those present in mammals, have not been identified in the teleost heart. Despite that an electrocardiogram with P, QRS, and T waves can be recorded (Satchell 1991), the teleost heart lacks a morphologically defined conduction system (Nair 1973; Sedmera et al. 2003). The absence of a regionalized pattern of connexin expression in the zebrafish (Christie et al. 2004) also argues against the presence of a conduction system in teleosts. It has been suggested that the geometry of the muscle trabeculae allows for the preferential spread of electrical excitation (Sedmera et al. 2003), thus being the functional correlate of the His-Purkinje system. The trabeculae anchored in the AV muscle ring (Fig. 2.7) may constitute that preferential pathway (Sedmera et al. 2003; Icardo and Colvee 2011).

Acknowledgments The author wishes to thank L. González and B. Gallardo for technical assistance.

References

- Beis D, Bartman T, Jin S-W, Scott IC, D'Amico LA, Ober EA, Verkade H, Frantsve J, Field HA, Wehman A, Baier H, Tallafuss A, Bally-Cuif L, Chen J-N, Stainier DYR, Jungblut B (2005) Genetic and cellular analyses of zebrafish atrioventricular cushion and valve development. *Development* 132:4193–4204
- Benjamin M, Norman D, Scarborough D, Santer RM (1984) Carbohydrate-containing endothelial cells lining the bulbus arteriosus of teleosts and the conus arteriosus of elasmobranchs (Pisces). *J Zool (London)* 202:383–392
- Burggren WW, Farrell A, Lillywhite H (1997) Vertebrate cardiovascular systems. In: Dantzler WH (ed) *Handbook of physiology*, sect 13, Comparative physiology, vol 1. Oxford University, New York, pp 215–308
- Caulfield JB, Borg TK (1979) The collagen network of the heart. *Lab Invest* 40:364–372
- Cerra MC, Canonaco M, Acierno R, Tota B (1997) Different binding activities of A- and B-type natriuretic hormones in the heart of two Antarctic teleosts, the red-blooded *Trematomus bernacchii* and the hemoglobinless *Chionodraco hamatus*. *Comp Biochem Physiol* 118A:993–999
- Cerra MC, Imbrogno S, Amelio D, Garofalo F, Colvee E, Tota B, Icardo JM (2004) Cardiac morphodynamic remodelling in the growing eel (*Anguilla Anguilla* L.). *J Exp Biol* 207:2867–2875
- Chang C-P, Neilson JR, Bayle JH, Gestwicki JE, Kuo A, Stankunas K, Graef IA, Crabtree GR (2004) A field of myocardial-endocardial NFAT signalling underlies heart valve morphogenesis. *Cell* 118:649–663
- Chen J-N, Fishman MC (2000) Genetics of heart development. *Trends Genet* 16:383–388
- Chen JN, van Eeden JM, Warren KS, Chin A, Nüsslein-Volhard C, Haffter P, Fishman MC (1997) Left-right pattern of cardiac *BMP4* may drive asymmetry of the heart in zebrafish. *Development* 124:4373–4382
- Christie TL, Muir R, White TW, Valdimarsson G (2004) Molecular cloning, functional analysis, and RNA expression analysis of connexin 45.6: a zebrafish cardiovascular connexin. *Am J Physiol* 286:H1623–H1632
- Durán AC, Fernández B, Grimes AC, Rodríguez C, Arqué JM, Sans-Coma V (2008) Chondrichthyan have a bulbus arteriosus at the arterial pole of the heart: morphological and evolutionary implications. *J Anat* 213:597–606
- Eastman JT (1993) *Antarctic fish biology. Evolution in a unique environment*. Academic, New York

- Eisenberg LM, Markwald RR (1995) Molecular regulation of atrioventricular valvuloseptal morphogenesis. *Circ Res* 77:1–6
- Farrell AP, Jones DR (1992) The heart. In: Hoar WS, Randall DJ, Farrell AP (eds) *Fish physiology*, Vol XII, The cardiovascular system, Part A. Academic, San Diego, pp 1–87
- Farrell AP, Hammons AM, Graham MS, Tibbits GF (1988) Cardiac growth in rainbow trout, *Salmo gairdneri*. *Can J Zool* 66:2368–2373
- Farrell AP, Johansen JA, Steffensen JF, Moyes CD, West TG, Suarez TK (1990) Effects of exercise training and coronary ablation on swimming performance, heart size and cardiac enzymes in rainbow trout, *Oncorhynchus mikiss*. *Can J Zool* 68:1174–1179
- Farrell AP, Simonot DL, Seymour RS, Clark TD (2007) A novel technique for estimating the compact myocardium in fish reveals surprising results for an athletic air-breathing fish, the Pacific tarpon. *J Fish Biol* 71:389–398
- Franco D, Markman MMW, Wagenaar GTM, Ya Y, Lamers WH, Moorman AFM (1999) Myosin light chain 2a and 2v identifies the embryonic outflow tract myocardium in the developing rodent heart. *Anat Rec* 254:135–146
- Greer Walker M, Santer M, Benjamin M, Norman D (1985) Heart structure of some deepsea fish (Teleostei: Macrouridae). *J Zool (London)* 205:75–89
- Grimes AC, Kirby ML (2009) The outflow tract of the heart in fishes: anatomy, genes and evolution. *J Fish Biol* 74:963–1036
- Grimes AC, Stadt HA, Sheperd IT, Kirby ML (2006) Solving an enigma: arterial pole development in the zebrafish heart. *Dev Biol* 290:265–276
- Harvey RP, Rosenthal N (1998) Heart development. Academic, San Diego
- He C-Z, Burch JBE (1997) The chicken GATA-6 locus contains multiple control regions that confer distinct patterns of heart region-specific expression in transgenic mouse embryos. *J Biol Chem* 272:28550–28556
- Horsthuis T, Christoffels VM, Anderson RH, Moorman AFM (2009) Can recent insights into cardiac development improve our understanding of congenitally malformed hearts? *Clin Anat* 22:4–20
- Hu N, Sedmera D, Yost HJ, Clark EB (2000) Structure and function of the developing zebrafish. *Anat Rec* 260:148–157
- Icardo JM (2006) Conus arteriosus of the teleost heart: dismissed, but not missed. *Anat Rec A* 288:900–908
- Icardo JM (2007) The fish endocardium. A review on the teleost heart. In: Aird WC (ed) *Endothelial biomedicine*. Cambridge University, Cambridge, pp 79–84
- Icardo JM, Colvee E (1998) Collagenous skeleton of the human mitral papillary muscle. *Anat Rec* 252:509–518
- Icardo JM, Colvee E (2011) The atrioventricular region of the teleost heart. A distinct heart segment. *Anat Rec* 294:236–242
- Icardo JM, Colvee E, Tota B (1996) Morphological organization of the sturgeon (*Acipenser naccarii*) heart with special reference to the collagenous architecture. In: VII International symposium on fish physiology, Oslo, Norway, 3–6 Aug 1996, p 93
- Icardo JM, Colvee E, Cerra MC, Tota B (1999a) Bulbus arteriosus of Antarctic teleosts. I. The white-blooded *Chionodraco hamatus*. *Anat Rec* 254:396–407
- Icardo JM, Colvee E, Cerra MC, Tota B (1999b) Bulbus arteriosus of Antarctic teleosts. II. The red-blooded *Trematomus bernacchii*. *Anat Rec* 256:116–126
- Icardo JM, Colvee E, Cerra MC, Tota B (2000a) Light and electron microscopy of the bulbus arteriosus of the European eel (*Anguilla anguilla*). *Cells Tissues Org* 167:184–198
- Icardo JM, Colvee E, Cerra MC, Tota B (2000b) The bulbus arteriosus of stenothermal and temperate teleosts: a morphological approach. *J Fish Biol* 57(suppl A):121–135
- Icardo JM, Colvee E, Cerra MC, Tota B (2002) The structure of the conus arteriosus of the sturgeon (*Acipenser naccarii*) heart: II. The myocardium, the subepicardium, and the conus-aorta transition. *Anat Rec* 268:388–398
- Icardo JM, Schib JL, Ojeda JL, Durán AC, Guerrero A, Colvee E, Amelio D, Sans-Coma V (2003) The conus valves of the adult gilthead seabream (*Sparus auratus*). *J Anat* 202:537–550

- Icardo JM, Brunelli E, Perrotta I, Colvee E, Wong WP, Ip YK (2005a) Ventricle and outflow tract of the African lungfish *Protopterus dolloi*. *J Morphol* 265:43–51
- Icardo JM, Imbrogno S, Gattuso A, Colvee E, Tota B (2005b) The heart of *Sparus auratus*: a reap-praisal of cardiac functional morphology in teleosts. *J Exp Zool* 303A:665–675
- Imbrogno S, Cerra MC, Tota B (2003) Angiotensin II-induced inotropism requires an endocardial endothelium-nitric oxide mechanism in the in-vitro heart of *Anguilla anguilla*. *J Exp Biol* 206:2675–2684
- Jones DR, Brill RW, Bushnell PG (1993) Ventricular and arterial dynamics of anaesthetised and swimming tuna. *J Exp Biol* 182:97–112
- Leknes IL (2009) Structural and histochemical studies on the teleostean bulbus arteriosus. *Anat Histol Embryol* 38:424–428
- Lepilina A, Coon AN, Kikuchi K, Holdway JE, Roberts RW, Burns CG, Poss KD (2006) A dynamic epicardial injury response supports progenitor cell activity during zebrafish heart regeneration. *Cell* 127:607–619
- Lohr JL, Yost HJ (2000) Vertebrate model systems in the study of early heart development: *Xenopus* and zebrafish. *Am J Med Genet* 97:248–257
- Midttun B (1983) Ultrastructure of the junctional region of the fish heart ventricle. *Comp Biochem Physiol* 76A:471–474
- Moorman AF, Christoffels VM (2003) Cardiac chamber formation: development, genes, and evolution. *Physiol Rev* 83:1223–1267
- Munshi JSD, Olson KR, Roy PK, Ghosh U (2001) Scanning electron microscopy of the heart of the climbing perch. *J Fish Biol* 59:1170–1180
- Nagai Y, Asaoka Y, Namae M, Saito K, Momose H, Mitani H, Furutani-Seiki M, Katada T, Nishina H (2010) The LIM protein Ajuba is required for ciliogenesis and left-right axis determination in medaka. *Biochem Biophys Res Commun* 396:887–893
- Nair MG (1973) The development of the nervous system in the heart of the Chinese carp, *Cyprinus carpio* (Linnaeus), with a special reference to its conduction system. *Mikroskopie* 29:1–7
- Niihori M, Mogami Y, Naruse K, Baba SA (2004) Development and swimming behaviour of medaka fry in a spaceflight aboard the space shuttle Columbia (STS-107). *Zool Sci* 21: 923–931
- Ohtani O (1987) Three-dimensional organization of the connective tissue fibers of the human pancreas. A scanning electron microscopic study of NaOH treated tissues. *Arch Histol Jpn* 50:557–566
- Parsons CW (1930) The conus arteriosus in fishes. *Q J Microsc Sci* 73:145–176
- Pieperhoff S, Bennett W, Farrell AP (2009) The intercellular organization of the two muscular systems in the adult salmonid heart, the compact and the spongy myocardium. *J Anat* 215:536–547
- Poss KD, Wilson LG, Keating MT (2002) Heart regeneration in zebrafish. *Science* 298:2188–2190
- Poupa O, Gesser H, Jonsson S, Sullivan L (1974) Coronary-supplied compact shell of ventricular myocardium in salmonids: growth and enzyme pattern. *Comp Biochem Physiol A* 48:85–95
- Priede IG (1976) Functional morphology of the bulbus arteriosus of rainbow trout (*Salmo gairdneri* Richardson). *J Fish Biol* 9:209–216
- Raso DS (1993) Functional morphology of laminin, collagen type IV, collagen bundles, elastin, and proteoglycans in the bulbus arteriosus of the white bass, *Morone chrysops* (Rafinesque). *Can J Zool* 71:947–952
- Rutenberg JB, Fischer A, Jia H, Gessler M, Zhong TP, Mercola M (2006) Developmental patterning of the cardiac atrioventricular canal by Notch and hairy-related transcription factors. *Development* 133:4381–4390
- Sánchez-Quintana D, Hurlé JM (1987) Ventricular myocardial architecture in marine fishes. *Anat Rec* 217:263–273
- Sánchez-Quintana D, Garcia-Martinez V, Climent V, Hurlé JM (1995) Morphological analysis of the fish heart ventricle: myocardial and connective tissue architecture in teleost species. *Ann Anat* 177:267–274

- Sans-Coma V, Gallego A, Muñoz-Chápuli R, de Andrés AV, Durán AC, Fernández B (1995) Anatomy and histology of the cardiac conal valves of the adult dogfish (*Scyliorhinus canicula*). *Anat Rec* 241:496–504
- Santer RM (1985) Morphology and innervation of the fish heart. *Adv Anat Embryol* 89:1–102
- Santer RM, Cobb JLS (1972) The fine structure of the heart of the teleost, *Pleuronectes platessa* L. *Z Zellforsch* 131:1–14
- Santer RM, Greer Walker M, Emerson L, Witthames PR (1983) On the morphology of the heart ventricle in marine teleost fish (teleostei). *Comp Biochem Physiol* 76A:453–457
- Satchell GH (1991) Physiology and form of fish circulation. Cambridge University, Cambridge
- Scherz PJ, Huiskens J, Shai-Hernandez P, Stainier DYR (2008) High-speed imaging of developing heart valves reveals interplay of morphogenesis and function. *Development* 135:1179–1187
- Schib JL, Icardo JM, Durán AC, Guerrero A, López D, Colvee E, de Andrés AV, Sans-Coma V (2002) The conus arteriosus of the adult gilthead seabream (*Sparus auratus*). *J Anat* 201:395–404
- Sedmera D, Reckova M, deAlmeida A, Sedmerova M, Biermann M, Volejnik J, Sarre A, Raddatz E, McCarthy RA, Gourdie RG, Thompson RP (2003) Functional and morphological evidence for a ventricular conduction system in zebrafish and *Xenopus* hearts. *Am J Physiol* 284:H1152–H1160
- Seternes T, Sorensen K, Smedsrod B (2002) Scavenger endothelial cells of vertebrates: a nonperipheral leukocyte system for high-capacity elimination of waste macromolecules. *Proc Natl Acad Sci USA* 99:7594–7597
- Shimada E, Kinoshita M, Murata K (2009) Expression of cardiac myosin light chain 2 during embryonic heart development in medaka fish, *Oryzias latipes*, and phylogenetic relationship with other myosin light chains. *Dev Growth Differ* 51:1–16
- Simoes K, Vicentini CA, Orsi AM, Cruz C (2002) Myoarchitecture and vasculature of the heart ventricle in some freshwater teleosts. *J Anat* 200:467–475
- Smith WC (1918) On the process of disappearance of the conus arteriosus in teleosts. *Anat Rec* 15:65–71
- Taneda Y, Konno S, Makino S, Morioka M, Fukuda K, Imai Y, Kudo A, Kawakami A (2010) Epigenetic control of cardiomyocyte production in response to a stress during the medaka heart development. *Dev Biol* 340:30–40
- Tota B (1978) Functional cardiac morphology and biochemistry in Atlantic bluefin tuna. In: Sharp G, Dizon A (eds) *The physiological ecology of tuna*. Academic, New York, pp 89–112
- Tota B (1989) Myoarchitecture and vascularisation of the elasmobranch heart ventricle. *J Exp Zool (Suppl)* 2:122–135
- Tota B, Garofalo F (2012) Fish heart growth and function: from gross morphology to cell signalling and back. In: Sedmera D, Wang T (eds) *Ontogeny and phylogeny of the vertebrate heart*. Springer, New York
- Tota B, Gattuso A (1996) Heart ventricle pump in teleosts and elasmobranchs: a morpho-dynamic approach. *J Exp Zool* 275:162–171
- Tota B, Cimini V, Salvatore G, Zummo G (1983) Comparative study of the arterial and lacunary systems of the ventricular myocardium of elasmobranch and teleost fishes. *Am J Anat* 167:15–32
- Tota B, Cerra MC, Mazza R, Pellegrino D, Icardo JM (1997) The heart of the antarctic icefish as paradigm of cold adaptation. *J Thermal Biol* 22:409–417
- Weber KT (1989) Cardiac interstitium in health and disease: the fibrillar collagen network. *J Am Coll Cardiol* 13:1637–1652
- Wong LYE, Moorman AF, Barnett P (2012) Basic cardiac development: the heart and its electrical components. In: Sedmera D, Wang T (eds) *Ontogeny and phylogeny of the vertebrate heart*. Springer, New York
- Yamauchi A (1980) Fine structure of the fish heart. In: Bourne G (ed) *Heart and heart-like organs*, vol 1. Academic, New York, pp 119–148
- Yelon D (2001) Cardiac patterning and morphogenesis in the zebrafish. *Dev Dyn* 222:552–563

Ontogeny and Phylogeny of the Vertebrate Heart

Sedmera, D.; Wang, T. (Eds.)

2012, X, 234 p., Hardcover

ISBN: 978-1-4614-3386-6