Radial polydactyly: putting together evolution, development and clinical anatomy

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Radial polydactyly: putting together evolution, development and clinical anatomy

Bríd Crowley[1], Susan Stevenson[1] and Rui Diogo[2]

Abstract

Evolutionary developmental pathology, a new biological field, connects the study of evolution, development and human pathologies. In radial polydactyly, traditional studies have focused mainly on skeletal anomalies. This study examines anatomical and operative records of 54 consecutive cases of radial polydactyly to investigate whether there is a consistent spatial correlation between muscles, tendons and bones and whether this reflects a link between the mechanisms that generate these structures. The data are explored in the context of two current models of limb development: the modularity and topology models. Autopod (hand) tendons and muscles are more predictable in terms of insertion site, supporting both topology and modularity models. Zeugopod (forearm) tendons are less predictable. Neither model universally predicts the anatomy in radial polydactyly. These observations provide evidence for the complexity of anatomy in radial polydactyly and the difficulty in predicting operative findings based on the level of skeletal duplication alone.

Keywords

Radial polydactyly, evolution, development, evolutionary developmental pathology (evo-devo-path), anatomy

Date received: 21st May 2018; revised: 27th September 2018; accepted: 29th September 2018

Introduction

Radial polydactyly presents with a range of skeletal and soft-tissue anomalies. Traditional studies have focused mainly on the skeletal anomalies as represented by the Wassel and Rotterdam classifications (Wassel, 1969; Zuidam et al., 2008). Little has been published about the anatomy of the tendons, muscles or other soft tissues (Marks and Bayne, 1978). Radial polydactyly has been a research interest of the first author for the past two decades. During primary surgery for radial polydactyly, highly variable soft-tissue anatomy both between and within Wassel groups has been observed. In particular, it has been found that skeletal level of duplication does not predict the soft-tissue anatomy. A greater understanding of the complex anatomy of radial polydactyly would aid surgical planning and may help prevent secondary deformity, but the question remains as to whether patterns can be predicted in radial polydactyly preoperatively. To explore this further, the field of investigation has been extended in collaboration with evolutionary developmental science.

Evolutionary developmental pathology (Evo-Devo-Path) is a new biological field that aims to connect the study of evolution, development and human pathologies (Diogo et al., 2015a, 2105b, 2016, 2017, 2018). An original component of this subfield is the study of model organisms to illuminate pathological conditions in humans and the study of pathological conditions in humans to test current developmental and evolutionary theories. Application of developmental models to clinical anatomical data provides a new perspective on musculoskeletal patterns and muscle–tendon–bone interactions. During limb

[1]Department of Plastic and Reconstructive Surgery, Royal Victoria Infirmary, The Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK
[2]Department of Anatomy, Howard University College of Medicine, Washington, DC, USA

Corresponding Author:
Bríd Crowley, Department of Plastic and Reconstructive Surgery, Royal Victoria Infirmary, The Newcastle upon Tyne Hospitals NHS Foundation Trust, Queen Victoria Road, Newcastle upon Tyne NE1 4LP, UK.
Email: brid.crowley@nuth.nhs.uk

development, the skeletal pattern precedes muscle pattern and thus the former could organize the latter. Various studies suggest that skeletal tissues may provide positional information for the subsequent development of soft tissues (Duprez, 2002; Duprez et al., 1999; Hurle et al., 1990).

Two current models connect the study of evolutionary developmental pathology to human conditions (Table 1). The first is the 'modularity model', which describes how in different parts of the limb, i.e. 'modules', tendon formation is dependent on different initiating factors during development. Huang et al. (2015), using the mouse model demonstrated that tendon development in the autopod (hand/foot) is cartilage-dependent, whereas zeugopod (forearm/leg) tendon anlagen have an induction, a muscle-independent phase, and an elongation, a muscle-dependent phase; and finally, there is a transient tendinous anlage linking the autopod and zeugopod tendons at the wrist (Havis et al., 2016; Huang et al., 2015) (Table 1).

The second model is the 'topology model' in which it is hypothesized that the muscle and tendon attachments are mainly related to topological positions rather than to the developmental identity of the digital ray on which they insert (Diogo and Abdala, 2010; Diogo et al., 2015a, 2015b, 2018). That is, in a human hand that lacks a thumb, the muscles that insert on the thumb are usually still present, inserting instead onto the index finger (Figure 1a). Also, in a trisomy-18 case with radial polydactyly, muscles that normally insert on the ulnar aspect of the thumb, e.g. the adductor pollicis, still insert on the ulnar duplicate whereas muscles that normally insert on the radial aspect of the thumb, e.g. the abductor pollicis brevis, insert on the radial duplicate (Figure 1b) (Table 1).

To test the validity of these two models, we have applied them to human data from anatomical operative records in radial polydactyly. We explore whether conclusions drawn from this exercise can guide clinical management by predicting anatomical findings preoperatively.

Methods

Fifty-four consecutive primary operations for radial polydactyly were undertaken by the first author using the same operative method. The Wassel classifications were noted and operation records constructed using the same headings to record the anatomical findings and the procedure undertaken. The skin envelope of the non-dominant duplicate was reflected and incisions were extended in a mid-lateral fashion on the dominant duplicate to give access to the underlying anatomy (Figures 2 and 3). Systematic recordings of operative anatomical findings and procedure were documented under the following headings: skin envelope; skeleton/joints; thenar muscles; extensor tendons; flexor tendons; and digital neurovascular bundle. Anonymized operative records of osteological and myological phenotypes were used to test the modularity and topology evolutionary developmental biology models as described above.

In testing the modularity model, we recorded the specific insertion sites of autopod and zeugopod tendons in radial polydactyly cases for the different skeletal phenotypes. Because the modularity model proposes different initiating factors for these two tendon types, we examined whether there was a difference in the clinical situation. The topology model proposes that, in radial polydactyly, tendons and muscles which normally have an insertion on the radial aspect of the thumb would insert on the radial duplicate and those which normally insert on the ulnar aspect of the thumb would insert on the ulnar duplicate. The clinical anatomical data were used to examine this theory.

Parental informed consent (written) was granted to use operative photos for publication.

Table 1. Models of limb development.

Modularity model	Topology model
Tendons formed from three modules (autopod, wrist and zeugopd)	Identity and attachment of limb tendons/muscles determined by topological position of digits on which they insert
Autopod tendons: cartilage dependent	Not determined by anlage or developmental identity of digits
Transient anlage tendons at wrist	Not determined by early developmental identity of bones/muscles
Zeugopod tendons: muscle dependent	
Huang et al., 2015	Diogo et al., 2015a, 2015b
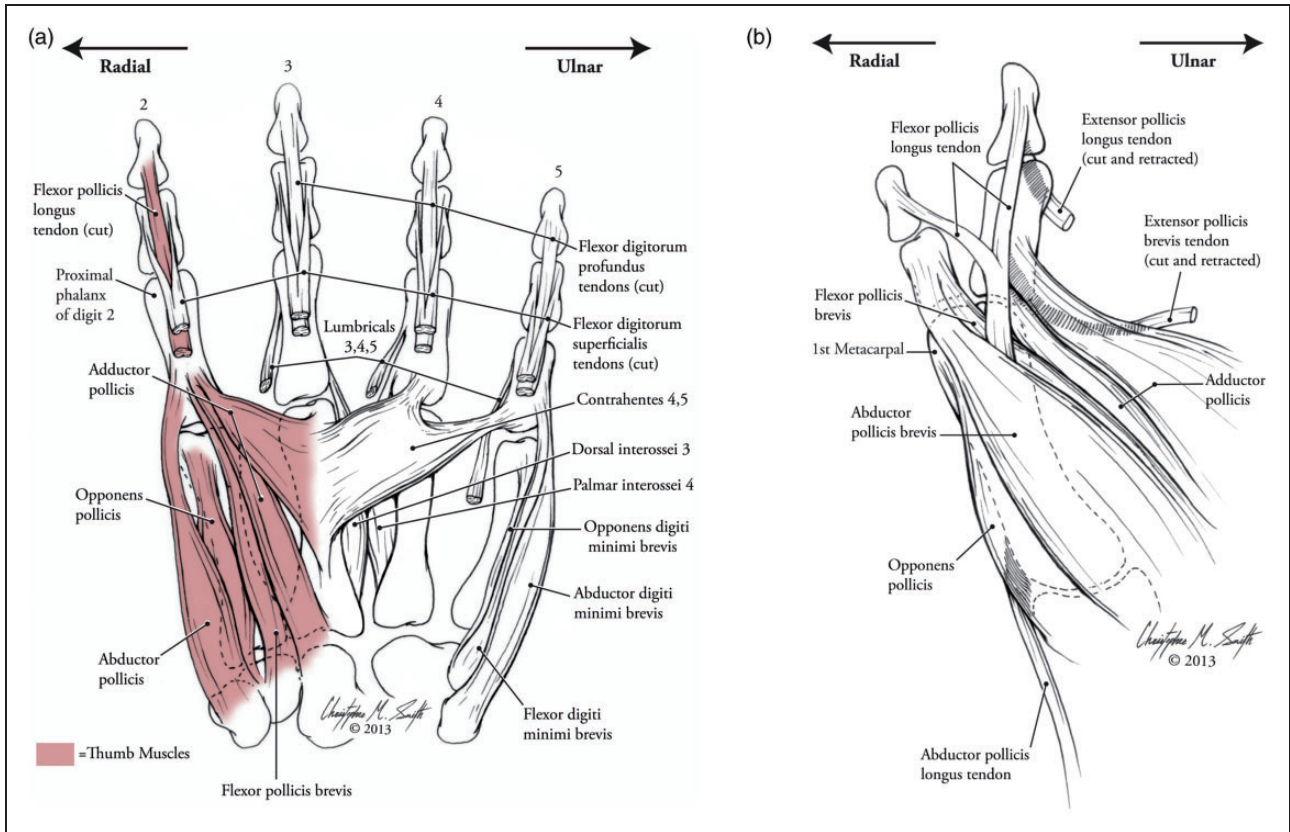
Figure 1. Anatomical findings in non-pentadactyl limbs in human with trisomy-18. (a) Hand lacks a thumb but thenar muscles insert onto digit 2 (index finger). (b) Radial polydactyly, muscles that normally insert on the ulnar aspect of the thumb insert on the ulnar duplicate, muscles that normally insert on the radial aspect of the thumb insert on the radial duplicate. (Copyright by Rui Diogo, co-author of this paper)

Figure 2. Wassel IV radial polydactyly (dorsal view). Skin envelope of radial duplicate reflected to explore extensor tendon anatomy. EPL is inserting on the ulnar duplicate. EPB is inserting on the radial duplicate. EPL: extensor pollicis longus; EPB: extensor pollicis brevis.
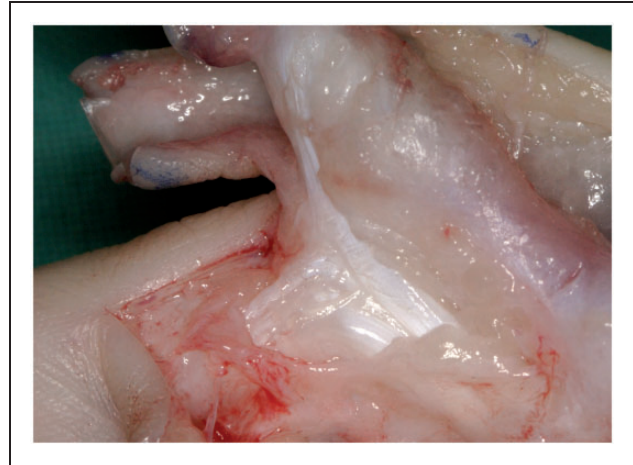
Figure 3. Wassel IV radial polydactyly (palmar view). Skin envelope of radial duplicate reflected to explore flexor tendon anatomy. FPL is bifurcating and inserting on both the ulnar and radial duplicates. FPL: flexor pollicis longus.
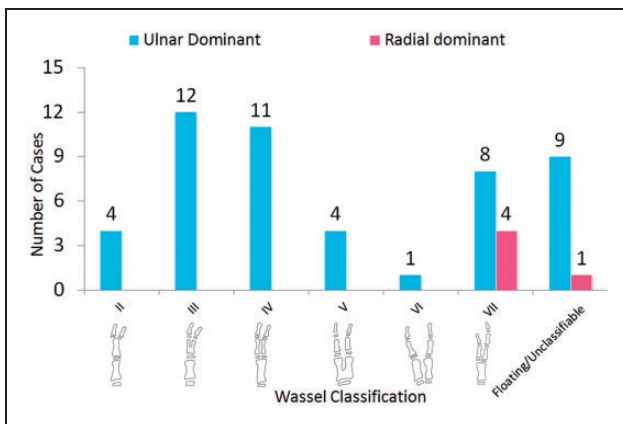
Results

Osteological phenotype

The ulnar duplicate was dominant in 49 cases and the radial duplicate in five (Figure 4). Radial polydactyly affected the right hand in 28 cases, the left in 12 cases and bilaterally in seven cases. Using the Wassel classification, ten cases were not classifiable, of which nine had a floating radial duplicate arising at or distal to the metacarpophalangeal joint and one had a floating ulnar duplicate arising at the metacarpal level.

Myological phenotype

The site of tendon/muscle insertion on bone was recorded for the extensor pollicis longus (EPL) (Table 2), extensor pollicis brevis (EPB) (Table 3), flexor pollicis

Figure 4. The dominant duplicate was ulnar in 49 cases, radial in five cases. Seven patients had bilateral hand involvement giving an overall total of 35 right hands and 19 left hands.

Table 2. Extensor pollicis longus (EPL) tendon insertion.

Wassel classification	Inserting both duplicates	Inserting ulnar duplicate only	Inserting radial duplicate only	EPL absent
II (n = 4)	3	1		
III (n = 12)	5	7		
IV (n = 11)	3	8		
V (n = 4)	1	3		
VI (n = 1)		1		
VII (n = 12)	7	5		
Unclassifiable (n = 10)	2	7		1

longus (FPL) (Table 4) and abductor pollicis brevis (APB) (Table 5). Other anomalies of tendons were documented for the extensor and flexor mechanisms (Tables 6–8). These data confirm that the anatomy in radial polydactyly is complex and variable. Two patients with similar osteological phenotype, e.g. Wassel IV, may have completely different myological phenotypes. Incorporating these data within the framework of our two evolutionary developmental biology models we observed the following:

- Intrinsic muscles of the hand (autopod) had more predictable spatial relationships of muscle–tendon–bone. APB insertion was proximal to the level of duplication in 16/54 cases. Of the remaining 38 thumbs, APB inserted on the topologically extra radial duplicate in most cases (30/38), even when this duplicate was non-dominant. This supports both the topology and modularity models, with exceptions. APB inserted on the ulnar duplicate only in eight thumbs in six of which the radial duplicate had no skeletal connection with the ulnar.

- Tendons arising from forearm (zeugopod) origins had less predictable configurations. One would expect the more ulnar EPL to insert on the ulnar duplicate in all cases but this occurred in only 32/54 thumbs, with insertions on both duplicates in 21/54 thumbs. EPB insertion was proximal to the level of duplication in nine of 54 cases, but absent in three. In the remaining 42 cases, the more radial EPB inserted on the radial duplicate only in 25 cases, the ulnar duplicate only in eight and both duplicates in nine. Variability was more marked in the triphalangeal subgroup, e.g. FPL inserted on the radial duplicate only in three of 12 triphalangeal cases; this pattern was not seen in the other osteological phenotypes.

Discussion

In evolutionary developmental pathology, predictions of the topology model of Diogo et al. (2015a, 2015b) match some aspects of the modularity model of Huang et al. (2015). Both support the idea that tendon formation in the autopod is cartilage-dependent. Early formation of cartilage-dependent intrinsic hand (autopod) tendons might be separate from that of muscle-dependent forearm (zeugopod) tendons, with these two types of tendon becoming associated at the level of the wrist at later stages of development. When combined, these models suggest a mode of limb development that is highly modular, flexible and evolvable. Human radial polydactyly, a common congenital hand difference, allows

Table 3. Extensor pollicis brevis (EPB) tendon insertion.

Wassel classification	Inserting both duplicates	Inserting ulnar duplicate only	Inserting radial duplicate only	Inserting proximal to level of duplication	EPB absent
II (n = 4)				4	
III (n = 12)		1	9	1	1
IV (n = 11)	3	1	6		1
V (n = 4)	1	1	2		
VI (n = 1)			1		
VII (n = 12)	1	2	6	2	1
Unclassifiable (n = 10)	4	3	1	2	

Table 4. Flexor pollicis longus (FPL) tendon insertion.

Wassel classification	Inserting both duplicates	Inserting ulnar duplicate only	Inserting radial duplicate only
II (n = 4)	4		
III (n = 12)	11	1	
IV (n = 11)	9	2	
V (n = 4)	3	1	
VI (n = 1)	1		
VII (n = 12)	3	6	3
Unclassifiable (n = 10)	3	7	

an opportunity to test the validity of these two models and potentially to draw conclusions that can guide clinical management by predicting the anatomical findings preoperatively.

The polydactyly cases summarized above and anatomical data available for other polydactyl tetrapods, demonstrate patterns that seem to favour the topology model. However, topology not only relates to the position of digits—an aspect emphasized by Diogo et al. (2015a, 2015b)—but also to size, longitudinal alignment and/or physical proximity of digits to the specific level where duplications arise. The latter has been reported by surgeons, but largely ignored by developmental biologists. In radial polydactyly, Marks and Bayne (1978) recorded patterns of forearm flexor and extensor configurations which were mainly consistent when taking into account the skeletal level of duplication. Thenar muscles attached to the radial duplicate thumb in all metacarpal and most proximal phalanx level duplications. Saito et al. (2018) suggested that thenar dysplasia in radial polydactyly depended on the level of bifurcation.

A similar scenario was described in the original study of 150 polydactyl cats by Danforth (1947). In a forelimb with six digits, the muscles inserting on the radial duplicate thumb were the muscles that insert on a normal thumb duplicate, whereas the muscles inserting on the ulnar duplicate were the muscles that normally insert on digit 2. This concurs with the topology model; the duplicated osteological and myological structures do not match.

Diogo et al. (2015a, 2015b) described this topological patterning in the six-digit hand of a trisomy-18 case (Figure 1b) in which muscles that normally insert on the ulnar aspect of the thumb inserted on the ulnar duplicate and those that normally insert on the radial side of the thumb inserted on the radial duplicate. They suggested that the muscles were 'blind' to the number of thumbs and developed in utero as if there would subsequently be a single digit ('super digit'). Our results support these findings, with APB inserting on the radial duplicate in most cases. Exceptions are seen in hypoplastic/floating radial duplicates where the APB inserts on the ulnar duplicate only (Table 5).

When Diogo et al. (2015a) proposed the topology model, exceptions were noted. Exceptions were also recorded by Danforth (1947) who demonstrated 'in cats of Type B (where instead of the thumb there is a long digit that resembles the index finger) there is frequently, but not always, a tendon to the radial digit'. Therefore, a certain 'type' of polydactyl osteological phenotype can be associated with different muscular patterns, something which is more evident in the long flexors and extensors. Our observations confirm that zeugopod muscles have less predictable configurations than autopod muscles. The more ulnar EPL inserts mainly on the ulnar thumb, the more radial EPB inserts mainly on the radial thumb, but there is variability (Tables 2 and 3). Long extensors/flexors that do not insert on the extra (radial) thumb seemingly contradict the topology model. However, our data also show that in most of those cases the radial thumb is nondominant, so it is possible that soft tissues such as these zeugopod muscles do not 'see' the radial thumbs and therefore do not insert or have a lesser

Table 5. Abductor pollicis brevis (APB) insertion.

Wassel classification	Inserting both duplicates	Inserting ulnar duplicate only	Inserting radial duplicate only	Inserting proximal to level of duplication
II (n = 4)				4[a]
III (n = 12)		1	5	6[a]
IV (n = 11)	4		6	1[b]
V (n = 4)	1		3	
VI (n = 1)			1	
VII (n = 12)		3	7	2[a]
Unclassifiable (n = 10)	2	4	1	3[a]

[a]APB inserting proximal phalanx.
[b]APB inserting first metacarpal.

Table 6. Extensor pollicis longus (EPL) anatomical variations.

Wassel classification	Eccentric insertion EPL	Hypoplastic EPL	Interconnections			Anomalous tendons
			Extensor to extensor	Extensor to flexor	Extensor to skin	
II (n = 4)						
III (n = 12)	4	2	1	5	1	1
IV (n = 11)	2			1		
V (n = 4)						
VI (n = 1)	1		1	1		
VII (n = 12)	3	1		2		2
Unclassifiable (n = 10)	1			2		1

Table 7. Extensor pollicis brevis (EPB) anatomical variations.

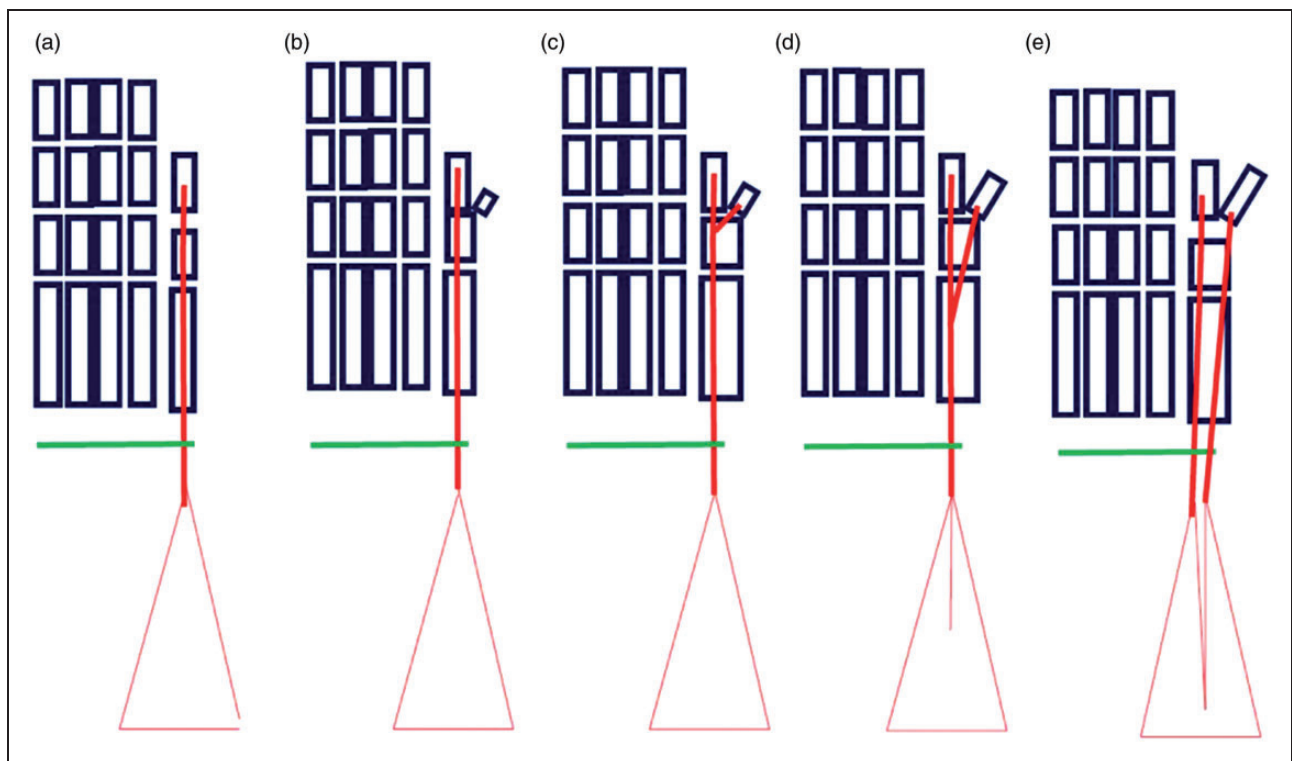| Wassel classification	Eccentric insertion EPB	EPB inserting distal phalanx radial duplicate, interconnection to FPL ulnar duplicate	Hypoplastic EPB	Anomalous origin EPB	Interconnections Extensor to extensor
II (n = 4)					
III (n = 12)	1		2		
IV (n = 11)	1	1			
V (n = 4)	1				
VI (n = 1)	1				
VII (n = 12)				1	
Unclassifiable (n = 10)					1

insertion on the radial thumb (Tables 2–4, Figure 5). In contrast, autopod muscles insert on the extra (radial) thumb even when this duplicate is non-dominant (Table 5).

One needs to be careful when saying that there is apparent randomness where the same osteological phenotype can be associated with different myological phenotypes. A detailed analysis, taking into account not only the number of digits, the number of phalanges of each digit and the level of skeletal bifurcation but also including the size and shape of bones, the connections and angles between them, and their topological position relative to muscles, may allow one to discern consistent patterns within what could at first sight seem a 'chaotic' scenario. This is supported by Danforth (1947) who

Table 8. Flexor pollicis longus (FPL) anatomical variations.

| Wassel classification | FPL insertion eccentric | Interconnections | | Deficient pulley system |
		Flexor to extensor	Flexor to flexor	
II (n = 4)	2		1	
III (n = 12)	10	5	4	6
IV (n = 11)	7	1	1	1
V (n = 4)				1
VI (n = 1)	1	1		
VII (n = 12)	2	2	2	
Unclassifiable (n = 10)	1	2		

Figure 5. Summary of a typical pattern seen by Danforth (1947) in the forearm/leg extensors/flexors inserting onto the autopods of polydactylous cats, applied to the human case using typical human osteology and a human muscle. Thick red line: tendon; green line: wrist level; triangle: muscle belly. (a) Normal configuration of extensor pollicis longus tendon and muscle belly. (b) Rudimentary extra radial thumb without tendons/muscle. (c–e) As the radial duplicate increases in size, the level of tendon bifurcation moves proximally to involve the muscle belly.

demonstrated that if two or more digits are so closely related that they form a so-called 'super-digit', tendons interpret the information as if there is a single digit, with a long tendon which might eventually divide and insert very distally on the individual digits. In contrast, when the muscles somehow 'see' a condition with two topologically clearly distinct digits, each of them resembling the normal digit, the tendon division is more proximal (Danforth, 1947). This led Danforth to suggest that the configuration of both the hard and soft tissues in cat polydactyly is 'far from random … for any given grade of polydactyly there was a degree of constancy that made it possible to predict with considerable accuracy what would be found in a second specimen of a type already dissected'. Danforth's
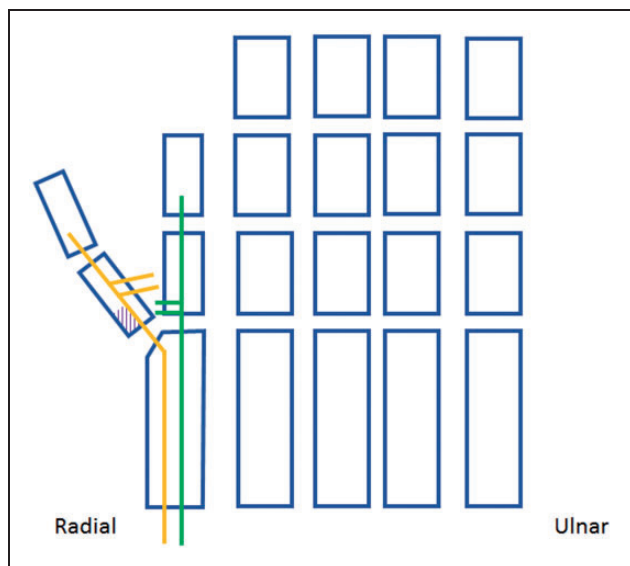
Figure 6. Dorsal schematic of Wassel IV duplication with dominant ulnar duplicate. EPL (green) inserting on the ulnar duplicate, anomalous insertion EPB (yellow) on distal phalanx of the radial duplicate. Tendon interconnections are shown. APB (cross-hatched) inserting on the radial base of the proximal phalanx.

conclusions support Alberch's (1989) 'logic of monsters' according to which even when evolution goes 'wrong', e.g in cases of birth defects, the system does not become random. There remains a 'logic', or a predictable order within the system.

Our observations and review of the literature reveal two important points:

- The majority of cases support the topology model and the autopod component of the modularity model. This is pertinent because it shows that one can predict, with a high degree of accuracy, the soft-tissue pattern of a patient associated with a specific skeletal pattern. Our clinical data seemingly contradict the zeugopod part of the modularity model.
- By showing exceptions to the more predictable norm, these data indicate that none of the models proposed so far is universal. The topology model is supported when it relates to the position of digits and the size, longitudinal alignment and/ or physical proximity of digits to the specific region where duplications arise.

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