

The trouble with flippers: a report on the prevalence of digital anomalies in Cetacea

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The forelimbs of cetaceans (whales, dolphins, and porpoises) are unique among mammals as the digits exhibit hyperphalangy, and the entire limb is encased in a soft tissue flipper that functions to generate lift. The typical morphology of cetacean digits has been well documented by detailed anatomical studies. This study however furthers our understanding of cetacean forelimb anatomy by conducting a taxonomically broad survey of cetacean digital anomalies. Forelimb radiographs from museum collections provided the basis upon which we calculated the prevalence and documented the morphology of cetacean digital abnormalities. Results indicated that 11% ($n = 255$) of toothed whales displayed some type of aberrant ossification: the majority of these cases displayed a fusion of elements within a single digital ray, whereas cases exhibiting branched digits were rare. A small sample of baleen whale radiographs ($n = 6$) contained the only documented case of baleen whale polydactyly in a specimen of the gray whale (*Eschrichtius*). Furthermore, some *Balaenoptera* specimens displayed ossified elements within the interdigital spaces that lacked attachment to the adjacent digits and carpus. In addition, we speculated on the role that several genes may have played in creating cetacean digital anomalies. © 2009 The Linnean Society of London, *Zoological Journal of the Linnean Society*, 2009, 155, 722–735.

ADDITIONAL KEYWORDS: flipper – forelimb – hyperphalangy – polydactyly – polyphalangy.

INTRODUCTION

Some vertebrates made the transition to a terrestrial lifestyle in the Devonian ~360 Myr. The transition from finned vertebrates to tetrapods with limbs consisted of several anatomical changes. The pectoral girdle evolved weight-bearing capabilities, and the bony elements of the manus became rearranged from linear radials to digits (Fig. 1A, B; Daeschler & Shubin, 1997; Shubin, Daeschler & Jenkins, 2006; Coates & Ruta, 2007). The earliest tetrapod, *Acanthostega*, had eight principal digits (Fig. 1B; Coates & Clack, 1990; Coates & Ruta, 2007), whereas subsequent terrestrial lineages of tetrapods exhibited a stable maximum of five manual digits (Fig. 1C, D).

Most phylogenies indicate that pentadactyly evolved only once (Coates & Ruta, 2007), and the presence of additional digits beyond the standard five (i.e. polydactyly) is usually considered to be anomalous. Furthermore, amniote digits evolved a stable phalangeal formula of 2/3/4/5/4, whereas mammals evolved a phalangeal formula of 2/3/3/3/3 (Fig. 1D; Fedak & Hall, 2004).

Two lineages of secondarily aquatic tetrapods radically altered their manus morphologies. Some Mesozoic marine reptiles (e.g. the ichthyosaur *Stenopterygius*) and modern cetaceans (whales, dolphins, and porpoises) increased the number of phalanges per digit beyond their ancestral digital formulas (Fig. 2B, hyperphalangy), encased the digits in a soft tissue flipper (Howell, 1930; Caldwell, 2002), and in some cases lost digit I (Motani, 1999; Cooper *et al.*, 2007). Hyperphalangy probably evolved in both

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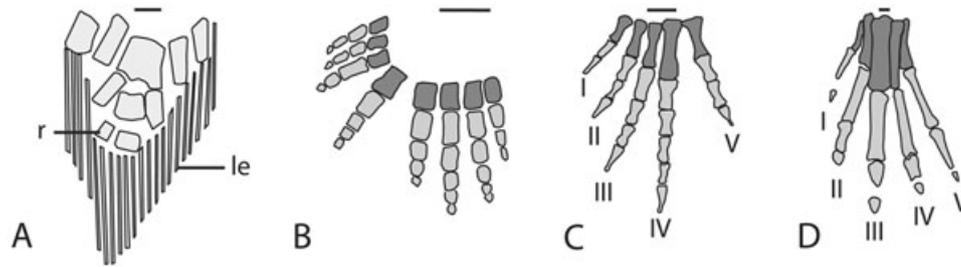


Figure 1. The evolution of digits among tetrapods. A, the early Devonian tetrapod *Tiktaalik* (Shubin *et al.*, 2006) with radials. B, *Acanthostega* (Coates & Clack, 1990) was the first tetrapod with digits. C, a synapsid (Carroll, 1988) displayed the canonical pentadactylous tetrapod manus. D, the pentadactylous archaeocete cetacean *Rodhocetus* displayed the primitive mammalian phalangeal formula of 2/3/3/3/3 (Gingerich *et al.*, 2001). Roman numerals indicate digit identity. Dark-grey elements are metacarpals, light-grey elements are phalanges. Radials (r) and lepitotrichia (le). Scale bars: 1 cm.

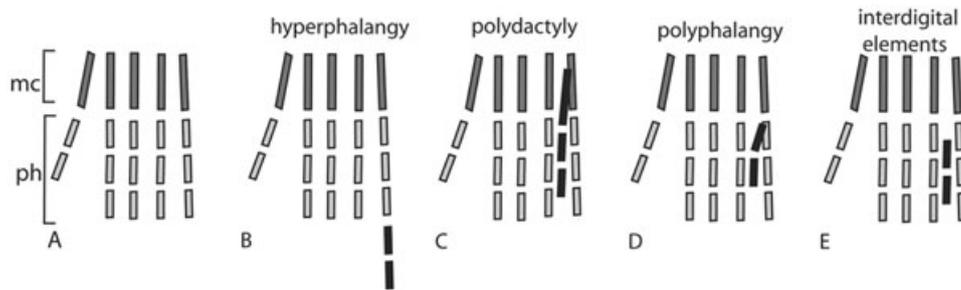


Figure 2. Illustrations of digital anomalies. A, the typical mammalian manus with five digits and a phalangeal formula of 2/3/3/3/3. B, hyperphalangy. C, polydactyly. D, polyphalangy. E, interdigital elements. Key: metacarpals (mc), dark grey; phalanges (ph), light grey; anomalous elements, black.

lineages as a functional consequence of using the flipper as an organ of steering or balance, rather than using the organ for propulsion (Richardson & Chipman, 2003). These two tetrapod lineages also display similar digital malformations, such as polyphalangy (Kükenthal, 1893; Burfield, 1920; Caldwell, 2002). This study, however, focuses on anomalies found in the cetacean manus.

Several detailed studies have documented the typical anatomy of the cetacean forelimb (e.g. Flower, 1885; Howell, 1930), but very few reports have documented cetacean digital anomalies. Two studies reported abnormal chondrification within the interdigital regions of some baleen (mysticete) whales (Fig. 3A; Kükenthal, 1893; Burfield, 1920). Within toothed whales (odontocetes), several varieties of digital anomalies have been documented. In the harbour porpoise (*Phocoena phocoena*), two abnormalities have been described. The first was an additional phalanx with modified chondroepiphyses that fused two digits together (Fig. 3B), and the second was a small and rounded accessory ossification (Fig. 3C; Kunze, 1912). Polydactyly was found to be a fixed trait in the vaquita porpoise (*Phocoena sinus*), possibly as the result of genetic drift following a

population bottleneck (Fig. 3D; Ortega-Ortiz, Villa-Ramirez & Gersenowies, 2000). A branched digit was reported in a single specimen of the bottlenose dolphin *Tursiops truncatus* (Fig. 3E; Watson, Stein & Marshall, 1994), and in several specimens of beluga whales (*Delphinapterus leucas*). Some belugas from a single population had a branched fourth digit (Fig. 3F), whereas a geographically separate population displayed a branched fifth digit (Kunze, 1912; Yablokov, 1974). Polydactyly was initially reported in the Amazon river dolphin (*Inia geoffrensis*, Pilleri & Gihl, 1976), but a review of its manus morphology indicated the presence of a carpal bone, not an additional digit (Watson *et al.*, 1994). Nothing is known of aberrant manual ossifications across baleen whales and more basal toothed whales (e.g. beaked whales).

In the rest of the skeleton, acquired abnormalities have been documented in response to trauma (e.g. Foley, 1979) or degenerative disease (e.g. Cowan, 1966; Turnbull & Cowan, 1999). Diagnostic features of degenerative disease include, but are not limited to, enthesiophyte (bony outgrowths specifically associated with ligament or synovial membrane attachments) and periarticular osteophyte (abnormal bone,

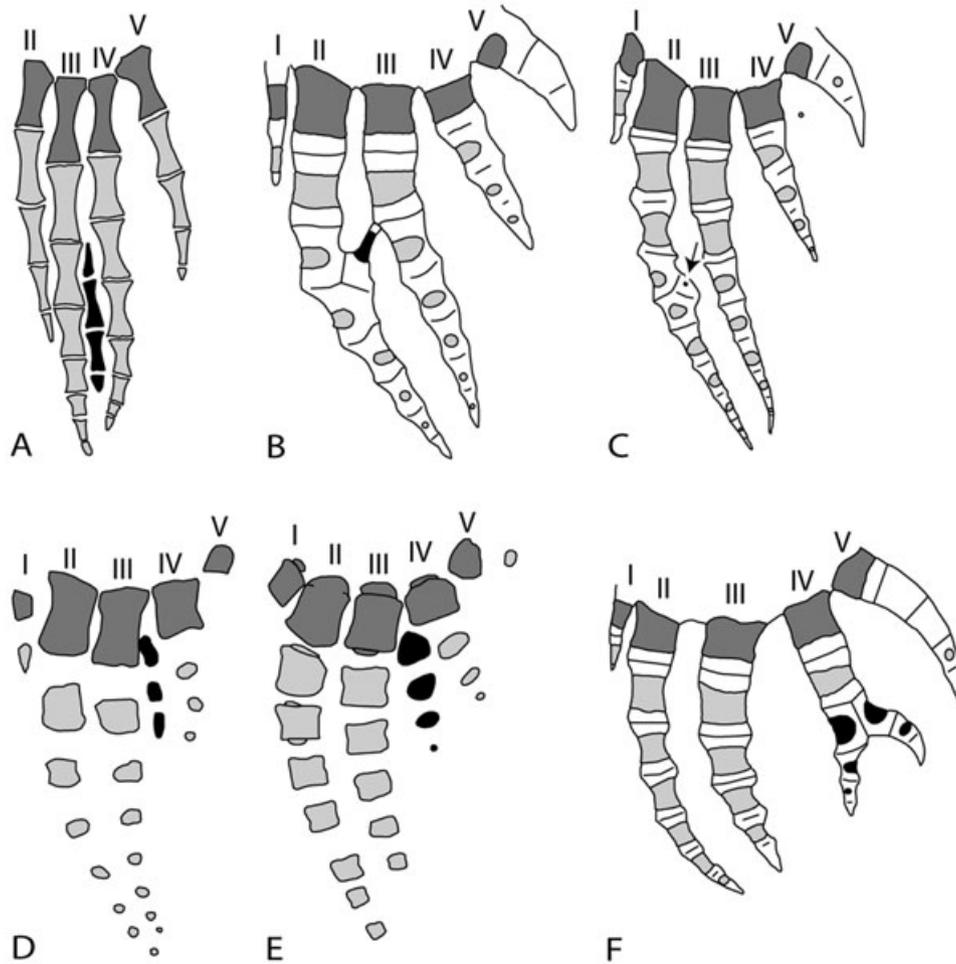


Figure 3. Published reports of cetacean digital malformations. A, cartilaginous interdigital elements in a fin whale (*Balaenoptera physalus*; Kükenthal, 1893). B and C, polyphalagy and an accessory ossification in two harbour porpoise (*Phocoena phocoena*; Kunze, 1912). D, polydactyly in the vaquita (*Phocoena sinus*; Ortega-Ortiz *et al.*, 2000). E, polyphalagy in a bottlenose dolphin (*Tursiops truncatus*; Watson *et al.*, 1994). F, polyphalagy in the beluga (*Delphinapterus leucas*; Yablokov, 1974). Illustrations are not drawn to scale. Roman numerals identify digits. Key: metacarpals, dark grey; phalanges, light grey; cartilages, white; anomalous elements, black.

or bone spur) formation (Allan, 2002), as well as ankylosis (Lagier, 1977; Turnbull & Cowan, 1999).

The objective of this study was to document the morphologies and prevalence of digital malformations in cetaceans. Based on the appearance and patterning of the pathology, we speculated on the mechanism generating it (i.e. developmental or acquired), and compared observed patterns to published accounts of digital malformations in other mammal groups and marine reptiles. Understanding cetacean digital malformations may thus allow insight into the prevalence of, and physiological responses to, digital trauma and disease. Finally, comparison of data from a large sample of cetaceans may help elucidate the developmental and genetic patterning of cetacean flippers.

MATERIAL AND METHODS

Radiographs of cetacean forelimbs offer a precise means of examining the position and morphologies of digital abnormalities. A total of 261 flipper radiographs, representing four species of baleen whales (mysticetes, $n = 6$) and twelve species of toothed whales (odontocetes, $n = 255$), were examined at the marine mammal collections of the Natural History Museum of Los Angeles County (LACM) and the National Museum of Natural History (USNM). For each odontocete specimen, the relative ontogenetic age was estimated (see below) and recorded. Because odontocetes strand frequently, and their forelimbs are small, collections are biased in their favour. Furthermore, adult mysticete forelimbs are typically

too large to radiograph easily, and therefore most mysticete radiographs are of ontogenetically young specimens.

DETERMINATION OF ONTOGENETIC AGE

To address whether some pathologies could be due to age-related conditions, relative ontogenetic age was estimated based on the degree of forelimb ossification. Epiphyseal fusion of the distal radius and ulna was used as an indicator of relative age in odontocete specimens. This technique has been explored in several species (i.e. Calzada & Aguilar, 1996; Dawson, 2003), and is useful for determining the relative age of odontocetes, but no such criteria have been established for mysticetes. Stages of fusion were described by Ogden, Conlogue & Rhodin (1981): stage 0, no radiographic evidence of a secondary centre of ossification; stage 1, a secondary centre of ossification is present, but the size is <50% of the metaphysis width; stage 2, the secondary centre of ossification is >50% of the metaphysis width; stage 3, the radiolucent physis (growth plate) is reduced in thickness; stage 4, there is some epiphyseal closure; stage 5, the epiphysis is closed, and is replaced by a radio-opaque line; stage 6, the epiphysis is closed, and the radio-opaque line is reduced to <50% of the metaphysis width. Accurate staging of epiphyseal closure is dependant on the exposure of the radiograph; it is not possible to determine the stage of fusion if the distal radius and ulna are underexposed. Therefore, whenever possible, specimens were also staged based on examination of osteological preparations.

DETERMINATION OF POLYDACTYLY AND POLYPHALANGY

We followed the terminology established by Johnson *et al.* (1982), Wise *et al.* (1997), Meteyer *et al.* (2000), and Fedak & Hall (2004) for describing digital anomalies (see Fig. 2). A digit is defined as consisting of only linearly arranged phalanges, and metacarpal elements are recognized as being separate from the digits. Most mammals have a phalangeal formula of 2/3/3/3/3, with digit I made of two phalanges and digits II–V made of three phalanges, but cetaceans are the only mammals that display greater than the plesiomorphic number of phalanges per digit (hyperphalangy, Howell, 1930; Cooper *et al.*, 2007). Polydactyly occurs when a metacarpal is duplicated, regardless of the number of phalanges. Polyphalangy refers to a digit with duplicated sets of phalanges. These duplicated phalanges may be the product of a mid-shaft split in the phalanges (creating branched elements), or from duplication at the interphalangeal joints. In the case of polyphalangy, duplicated pha-

langes lie adjacent to other phalanges, whereas in hyperphalangy additional phalanges are added linearly at the tips of the digits (Richardson & Oelschläger, 2002). Here, we describe a digital anomaly in which a series of elements lie in the interdigital space of a flipper, and these elements are unattached to the carpus, metacarpals, and adjacent phalangeal elements (Fig. 2E).

MANUS ABNORMALITIES

This study covers two broad categories of abnormalities: developmental and acquired. Developmental abnormalities may generate duplicated phalanges or digits, or the loss of elements, and may be caused by changes in the genes responsible for patterning and ossification of the skeleton, as well as by alterations in developmental pathways caused by the presence of a teratogen (Dabin *et al.*, 2004). Acquired conditions can cause proliferation or resorption of bone resulting from pathological conditions such as trauma, or degenerative or metabolic disease (osteoarthritis), and often include enthesiophyte and periarticular osteophyte formation, as well as ankylosis (Allan, 2002). We also suggest whether the flipper pathologies were possibly derived from developmental or acquired conditions, and the relative frequency of these two categories was then compared. This study also differentiated accessory centres of ossification from polyphalangy if the anomalous element did not match the shape of, and was smaller than, an adjacent phalanx.

RESULTS

POLYDACTYLY

Radiographs of a neonatal specimen of a grey whale (*Eschrichtius robustus*, LACM 54543) document the first case of polydactyly within the suborder Mysticeti (baleen whales). The specimen was a male, with a total length of 508 cm, collected on 31 January 1974 from Puerto Santo Domingo, Baja California Norte, Mexico by D.R. Patten. A polydactylous digit, associated with digit IV, was found in the right flipper (Fig. 4A, B). This additional digit consisted of a single reduced accessory metacarpal nested within an enlarged cartilage shared with metacarpal IV, and three accessory phalanges adjacent to digit IV. The anomalous element adjacent to metacarpal IV was rounded like a carpal element, and was much smaller than the metacarpals. Metacarpal IV was delta-shaped with a convex posterior aspect, and was apposed to the rounded margin of the accessory rounded bone. This morphology resembled the 'kissing delta' phalanx condition described in accounts

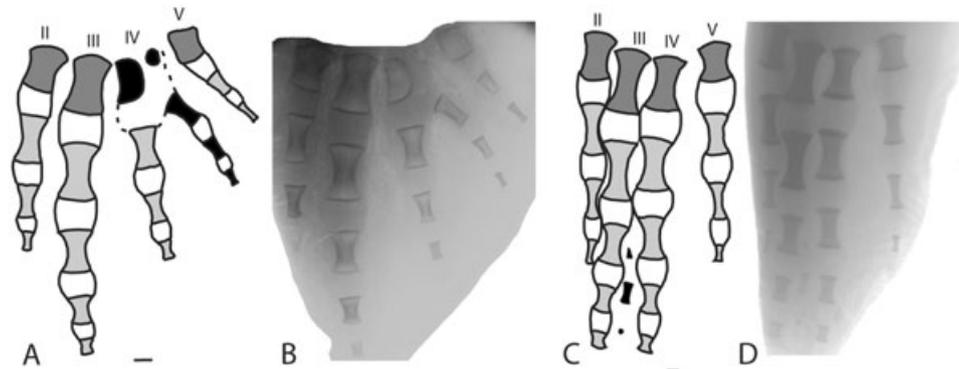


Figure 4. Tracing (A) and radiograph (B) of the right flipper of a grey whale (*Eschrichtius robustus*, LACM 54543). An additional digit lies between digits IV and V, and is represented by a single rounded metacarpal and three phalanges. The dotted line indicates the extent of cartilage shared between digit IV and the anomalous digit. Tracing (C) and radiograph (D) of the flipper of a fin whale (*Balaenoptera physalus*, USNM 550116). Three additional phalanges are embedded in the connective tissue between digits IV and V. Scale bars: 1 cm. Key: metacarpals, dark grey; phalanges, light grey; cartilages, white; anomalous elements, black.

of human polydactyly (Dawson, 2003; Elliot *et al.*, 2004). The additional phalanges have hourglass-shaped diaphyses, and were intermediate in size compared with the adjacent phalanges, indicating that this extra digit was not an identical or mirror image duplication of adjacent digits.

OSSIFIED ELEMENTS IN THE INTERDIGITAL SPACES

This study documents the first two cases of ossified interdigital elements in mysticetes. Previous documentation of this anomaly reported only cartilaginous elements (Fig. 3A; Kükenthal, 1893; Burfield, 1920). The first specimen to show anomalies (USNM 550116, male, total length 730 cm) was collected on 29 January 1982, 0.75 m east of Ramp 34, Buxton, Dare County, North Carolina, USA by R.G. Dagit. Another specimen to show digital anomalies (USNM 550115, male, total length 495 cm) was collected on 23 January 1982, 0.2 m north of Avon Pier, Avon, Dare County, North Carolina, USA by J.G. Mead. A radiograph of the neonatal fin whale (*Balaenoptera physalus*, USNM 550116) showed a series of ossified phalanges located in the interdigital space between digits III and IV, that lacked attachment to the other cardinal bones (Fig. 4C, D). The proximal phalanx was cone-shaped, with the apex directed proximally. The larger middle phalanx was hourglass-shaped, whereas the distal and smallest phalanx was ovoid. Adjacent digital elements were normal in morphology. The second case was found in the left flipper of a neonate fin whale (*B. physalus*, USNM 550115), which was similar to the interdigital elements found in the other neonatal *B. physalus* specimen (USNM 550116). The left flipper of USNM 550115 displayed a

single ossified rectangular-shaped phalanx lying between digits III and IV, at the level of phalanx 2.

ABNORMAL PATTERNS OF OSSIFICATION

Of the 255 radiographs of odontocete forelimbs examined in this study, approximately 11% (28 specimens) showed varying degrees of abnormal ossification within the digital rays (Table 1). Out of the 28 anomalies, 24 were considered to be developmentally derived conditions, whereas four exhibited morphologies similar to the acquired condition of degenerative joint disease (Table 2). In addition to polydactyly and polyphalangy, anomalies included metacarpophalangeal fusion (Fig. 5G, H), phalangeal fusion (Fig. 5A, B, G, H), and accessory centres of ossification near the metacarpals and phalanges of the principal digits (Fig. 5C, D). Ankylosis of the interphalangeal joints was the most common pathology, as 16 occurrences were documented in 28 anomalous specimens, mostly within digits I–III (Tables 1 and 3). Metacarpophalangeal fusion was documented in 12 cases, and was most frequently observed within digital rays I and IV. The only odontocete to fuse the joints of digital ray V (metacarpal V–phalanx 1 fused; phalanges 2–3 fused) was a single beaked whale, *Mesoplodon europaeus* (Fig. 5G, H; Table 1, USNM 504256).

The odontocete family Delphinidae (dolphins) displayed the greatest number of digital anomalies, and was the only family to show pathologies clearly associated with the acquired condition of degenerative joint disease. Of the 16 observed radiographs of the dolphin *Steno*, four individuals (25%) showed pathologies consistent with degenerative joint conditions

Table 1. Digital anomalies found in the odontocetes (toothed whales) at the National Museum of Natural History (USNM)

Taxon	USNM number	Stage	Total length (cm)	Anomaly
Kogiidae – pygmy sperm whales				
<i>Kogia breviceps</i> (n = 13)	504318	?	288	III, ph 4–5 fused; V, ph 1–2 fused
	550350	?	274	II, ph 2–3 fused; abnormalities present
<i>Kogia sima</i> (n = 1)	550482	4	213	II, accessory ovoid bone between ph 2 and 3, both flippers (Fig. 5C, D)
Ziphiidae – beaked whales				
<i>Mesoplodon europaeus</i> (n = 3)	504256	6	473	mc V-ph 1 fused; V, ph 2–3 fused (Fig. 5G, H)
Delphinidae – dolphins				
<i>Delphinus delphis</i> (n = 67)	500261	5	186	mc IV-ph 1 fused in one flipper; I, ph 1–2 fused in other flipper
	500356	5	175	I, ph 1–2 fused
	550041	?	200	I, ph 1–2 fused (Fig. 5A, B)
	550808	5	210	I, ph 1–2 fused
	550864	5	222	I, ph 1–2 fused, both flippers; mc IV-epiphysis of ph 1 fused
	571398	5	232	II, accessory ossification between ph 3 and 4
	571399	?	215	I, ph 1–2 fused, in one flipper; I, elongated distal-posterior aspect of ph 1 in other flipper
<i>Feresa attenuata</i> (n = 1)	550389	5	208	mc I-ph 1 fused, both flippers
<i>Lagenorhynchus acutus</i> (n = 43)	484914	5	243	V, accessory ossification
<i>Lagenorhynchus albirostris</i> (n = 1)	550208	?	238	I, mc I-ph 1 fused, both flippers
<i>Steno bredanensis</i> (n = 16)	504461	4	202	I, mc I-ph 1 fused, both flippers
	504462	6	215	mc IV and mc V fused
	504468	6	227	mc I and ph1 elongated along anterior aspect; II, ph 2–6 elongated/fused along anteroposterior joint surface; III, ph 1–5 anteroposterior elongation with partial bony fusion (Fig. 6)
	550221	6	215	II, ph 3–4 fused anteroposteriorly; II, anteroposterior elongation of ph 4 and 5
	550368	6	208	II, ph 3–6 fused anteroposteriorly both flippers; III, ph 1–4 elongated or fused along anterior aspect, one flipper; III, ph 1–3 elongated along anterior aspect but not fused, one flipper
	550837	5	228	II, ph 4–6 elongated along anterior aspect; III, ph 3 and 4 elongated along anterior aspect
<i>Stenella attenuata</i> (n = 7)	550016	6	193	IV, mc IV-ph 1 fused, both flippers; III, ph 1–2 fusion, one flipper
<i>Stenella coeruleoalba</i> (n = 22)	500837	?	194	I, mc I-ph 1 fused
	500838	?	206	I, mc I-ph 1 fused, both flippers
	550495	6	220	I, mc I-ph 1 fused, both flippers
<i>Stenella frontalis</i> (n = 5)	504736	5	210	V, additional metacarpal ossification centre (Fig. 5E, F)
	550376	5	216	V, additional metacarpal ossification centre
	550748	?	205	mc IV-ph 1 fusion
<i>Tursiops truncatus</i> (n = 76)	571173	4	211	mc III-ph 1 fusion

Abbreviations: mc, metacarpal; ph, phalanges.

Roman numerals indicate digit number.

Total length (cm) refers to body length, not flipper length.

Table 2. Prevalence of digital anomalies in odontocete taxa with large sample sizes

Taxon	<i>n</i>	Percentage with digital anomalies	Percentage with degenerative morphologies
<i>Delphinus delphis</i>	67	10%	0%
<i>Lagenorhynchus acutus</i>	43	2%	0%
<i>Steno bredanensis</i>	16	12%	25%
<i>Stenella coeruleoalba</i>	22	13%	0%
<i>Tursiops truncatus</i>	76	1%	0%

(Table 2; Fig. 6A, B). These individuals showed isolated lengthening of phalanges along the anterior, and sometimes posterior, edges of digits III and IV. This localized bony lengthening leads to joint fusion along the anterior–posterior edges (Table 1), but fusion was incomplete as the joint centres remained cartilaginous, and each element lacked ossified epiphyses. In addition to the condition of phalangeal fusion found in *Steno*, the first two phalanges of digit I were fused in six individuals of *Delphinus*. Ankylosis of these joints had a different presentation than that of *Steno*, given that the gross radiographic appearance showed more rugose bone formation, and new bone formation was not limited to the anterior and posterior margins of the digits. It was not clear from the radiographs if the osteophytes were truly periarticular, or if there was some bony bridging involving the articular surface of the joint itself. These bony changes were probably consistent with degenerative joint disease. Of the Delphinidae, *Lagenorhynchus acutus* and *T. truncatus* exhibited the fewest pathologies (Tables 1 and 2).

In our database, bone fusion was only noted in radiographically mature odontocetes. All specimens of *Steno*, which show periarticular osteophytes on the anterior and posterior phalangeal joint margins, were at distal radial–ulnar epiphyses fusion stage 4 or above (total body length 208 cm or greater). Other delphinids noted to have phalangeal fusion in the first digit were all at distal radial–ulnar epiphysis fusion stage 5 or 6. These data were consistent with either primary or secondary degenerative joint disease.

An additional bone was found in *Kogia breviceps* (Fig. 5C, D; Table 1, USNM 550482) along the anteriormost aspect of digit II, in the phalanx 2–3 interphalangeal joint. This accessory bone was circular, and the phalanx proximal to it had proximo-anterior elongation. A similar accessory bone was found in digit II of *Delphinus delphis* (USNM 571398), but was much smaller in diameter. Two specimens of *Stenella frontalis* (USNM 504736, 550376) displayed two dis-

tinct ossification centres for metacarpal V (Fig. 5E, F), whereas the surrounding elements appeared to have a normal morphology.

DISCUSSION

OSSIFIED ELEMENTS IN THE INTERDIGITAL SPACES

Mysticetes exhibit two manus morphologies: balaeids (right and bowhead whales) are pentadactylous, whereas all other mysticetes (grey, pygmy right, and rorqual whales) are tetradactylous, as they lack digit I (Cooper *et al.*, 2007). This study confirms earlier reports that some tetradactylous rorqual whales (*B. physalus* and *Balaenoptera musculus*) possess cartilaginous phalanges located in the middle interdigital space (Fig. 3A; Kükenthal, 1893; Burfield, 1920). In addition to confirming the presence of interdigital elements, this study documents ossification of these interphalangeal elements based on two specimens of fin whales (*B. physalus*, USNM 550115, 550116; Fig. 4C, D).

Cartilaginous elements located within the interdigital spaces of mysticetes (Fig. 3A) were originally interpreted as remnants of a missing digit in tetradactylous mysticetes (Kükenthal, 1893; Burfield, 1920). Subsequent hypotheses interpreted these phalanges as anomalous, rather than atavistic (Howell, 1930), and recent testing of these hypotheses has shown that the presence of these chondrified elements are in fact anomalous, and offer no evidence regarding digit identity (Cooper *et al.*, 2007).

In this study, we document the first ossifications of interdigital elements. These elements are located near a digit, but bear no direct attachment (bony or cartilaginous) to the carpus, metacarpals, or adjacent phalangeal series. Furthermore, these elements are held in place by a network of dense interdigital connective tissue, and may lie in the interdigital spaces (Fig. 4C, D), or along the margins of the manus. It is not currently possible to identify whether the interdigital elements represent metacarpals or phalanges.

Interdigital elements with similar locations within the manus have been documented in other secondarily aquatic tetrapods. Linear arrangements of interdigital elements occurred in fossil ichthyosaurs (Motani, 1999; Caldwell, 2002) along either the posterior margin of the flipper, or between the cardinal digits. These elements could be interpreted as remnants of a bifurcated digit, indicating polyphalangy, or anomalous interdigital ossifications. In the absence of diagnostic soft-tissue information, we conservatively describe the supernumerary rows of phalanges in some ichthyosaurs as evidence of branched digits, but recognize that these elements may bear a similar

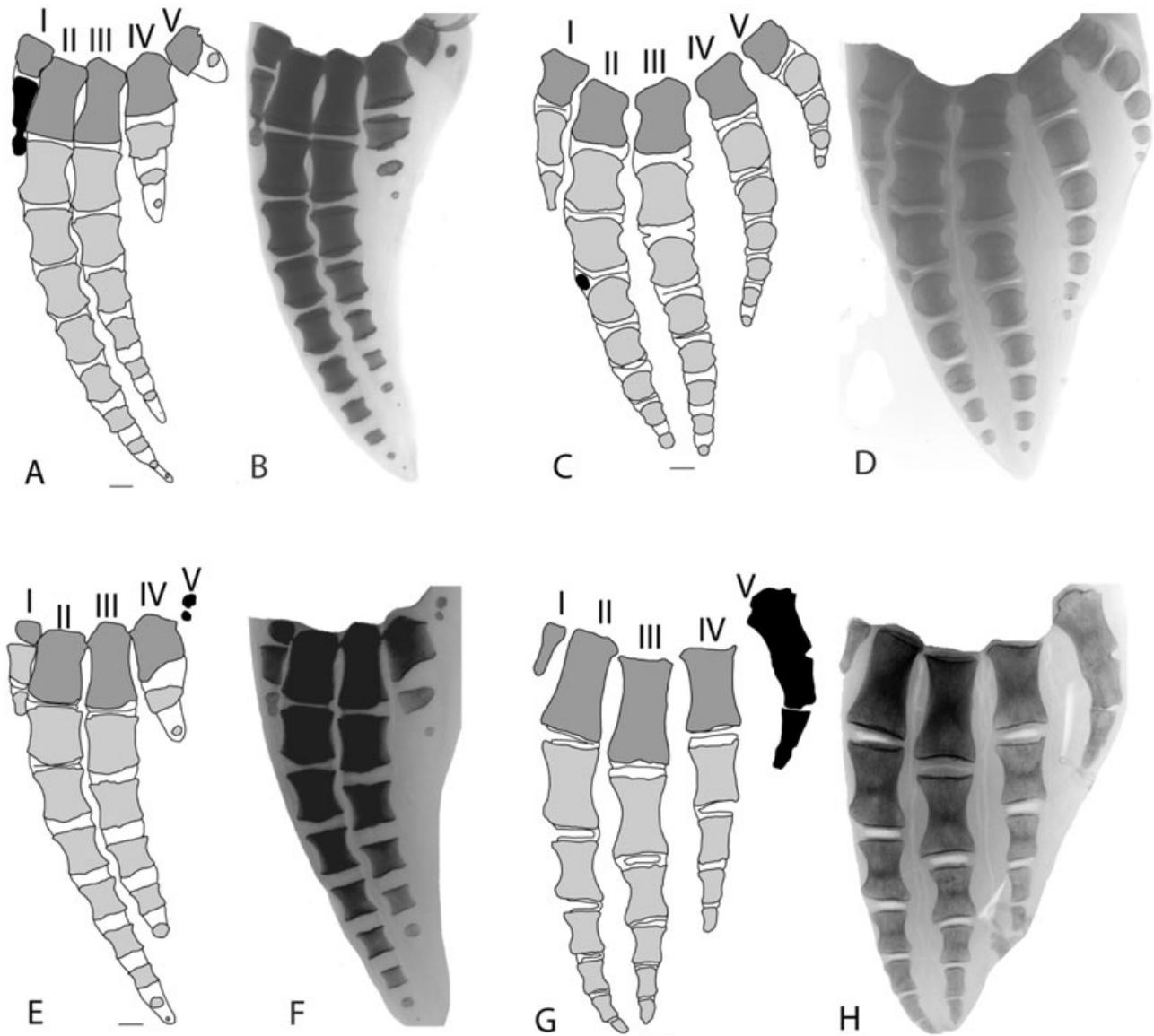


Figure 5. Phalangeal fusion in tracing (A) and radiograph (B) of a common dolphin (*Delphinus delphis*, USNM 550041). C and D, accessory ossification in a dwarf sperm whale (*Kogia sima*, USNM 550482). E and F, additional metacarpal ossification centre in an Atlantic spotted dolphin (*Stenella frontalis*, USNM 504736). G and H, metacarpal–phalangeal and interphalangeal fusion in Gervais' beaked whale (*Mesoplodon europaeus*, USNM 504256). Scale bars: 1 cm. Key: metacarpals, dark grey; phalanges, light grey; cartilages, white; anomalous elements, black.

morphology to the aberrant ossifications seen in balaeopterid cetaceans.

COMPARISONS

Current molecular and morphological studies place cetaceans within Artiodactyla (e.g. Gingerich *et al.*, 2001; Boisserie, Lihoreau & Brunet, 2005; Thewissen *et al.*, 2007), and it is therefore useful to compare cases of cetacean anomalies with those of terrestrial artiodactyls. The weight on most artiodactyl feet is

borne by digits III and IV, whereas digits I, II, and V are reduced or absent, and usually do not touch the ground during locomotion (Prentiss, 1903). Artiodactyl polydactyly and polyphalangy are most frequently reported in association with the reappearance and bifurcation of digits I and II (e.g. *Sus scrofa*, *Cervus* spp., *Rangifer*, *Bos*, *Ovis*; Prentiss, 1903; Miller & Broughton, 1971; Leipold, Dennis & Huston, 1972), and sometimes these additional digits are robust enough to be loaded, whereas in others they are just an atavistic digit that serves no obvious purpose

Table 3. Cetacean digital anomalies

Taxon	Polydactyly	Polyphalangy	Anomalous centres of ossification	Metacarpophalangeal fusion	Interphalangeal fusion	Reference
Odontoceti (toothed whales)						
<i>Kogia</i>			II	V	II, III, V	This study
<i>Mesoplodon europaeus</i>					V	This study
<i>Delphinapterus</i>		IV*, V*				Yablokov (1974)
<i>Phocoena phocoena</i>		II	II			Kunze (1912)
<i>Phocoena sinus</i>			II		I (6)	Ortega-Ortiz <i>et al.</i> (2000)
<i>Delphinus delphis</i>	III*			IV (2)		This study
<i>Feresa attenuata</i>			V	I		This study
<i>Lagenorhynchus</i>				I		This study
<i>Steno bredanensis</i>				I	II (3), III (2)	This study
<i>Stenella attenuata</i>				IV	III	This study
<i>Stenella coeruleoalba</i>				I (3)		This study
<i>Stenella frontalis</i>			V (2)	IV		This study
<i>Tursiops truncatus</i>		III		III		Watson <i>et al.</i> (1994); this study
Mysticeti (baleen whales)						
<i>Balaenoptera</i>		ip (4)				Kükenthal (1893); Burfield (1920); this study
<i>Eschrichtius</i>	IV					This study

The digit number is shown in roman numerals; ip, interdigital polyphalangy.

*Indicates taxa with an abundance of this morphology within the sample.

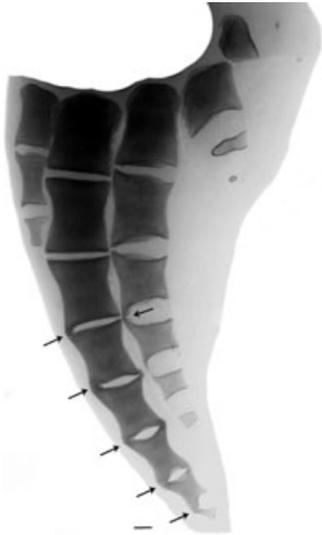


Figure 6. Radiograph of the flipper of a rough-toothed dolphin (*Steno bredanensis*, USNM 504468). Metacarpal I and phalanx 1 are elongated. Phalanges of digits II and III are elongated, and are frequently fused along their anterior aspects (black arrows), and less frequently along their posterior aspects. Scale bar: 1 cm.

during locomotion (Prentiss, 1903). Contrary to this regionalized expression of additional elements associated with digits I and II in artiodactyls, cetacean accessory elements were observed in association with the more posterior digits II and V. Furthermore, cases of polydactyly and accessory interdigital elements in cetaceans were associated with more central digits (III and IV), rather than the terrestrial artiodactyl-like condition of anomalies associated with the anterior digits (I and II).

DEGENERATIVE JOINT DISEASE IN *STENO*

Bony changes in the phalanges of *Steno* may be described as periarticular osteophytes and enthesiophytes. In domestic animals, radiographic manifestations of these lesions are typically used as indicators of degenerative joint disease (DJD) (Allan, 2002). DJD may be primary (age-related alteration of normal joint morphology) or secondary (as a result of acute or chronic trauma, infection, or developmental anomaly of a joint). Because the interphalangeal joints in cetaceans are not necessarily cavitated synovial joints, the classic definition of DJD may not apply. The condition that leads to fusion of phalanges may be better defined by a (new) term unique to the synchondroses found in cetaceans, such as cetacean synovial joint diseases (Turnbull & Cowan, 1999).

Classic DJD includes cartilage changes, which occur before there is any radiographic evidence of disease. The resolution on these radiographs may be

insufficient to evaluate subchondral bone lesions. This study is therefore limited to identifying pathology based on radiographic diagnosis, rather than the more precise techniques of histopathology. However, this limitation implies that only advanced, grossly detectable lesions are identified, and that the incidence of bone and joint pathology is underestimated in this study.

It is probably not possible, without evidence other than radiographs, to distinguish between primary and secondary causes of DJD in cetacean flippers. The *Steno* specimens examined were all osteologically mature animals, which implied either primary DJD or chronic trauma. There was no evidence of bone fracture in any of the flipper radiographs, and phalangeal fusion may have been a result of age-related, primary DJD. In some odontocetes, phalangeal fusion may have been a 'normal' consequence of ageing. Periarticular osteophytes and enthesiophytes may have formed as a result of chronic microtrauma to the joint capsules and tendons that course along the interphalangeal joints.

Excessive bending of the *Steno* flipper may have caused chronic connective tissue strain, and triggered a cascade of events that resulted in new bone formation and bony fusion to stabilize these joints. If the leading edge of the *Steno* flipper was subject to hydrodynamic forces that caused the distal flipper to bend caudally, tensile stresses may have concentrated on the leading edge (cranial border) of these distal cartilaginous joints, joint capsules, and associated tendons. In response to periodic tensile stresses, cartilage growth accelerates and is replaced by bone (Carter & Wong, 2003; Carter *et al.*, 2004). Therefore, ossification on the leading edges of *Steno* joints may have been the mechanobiological response of the individual joints to intermittent hydrodynamic stresses. Ossification of the joint edges in *Steno* may have functioned to immobilize these joints.

DEVELOPMENTAL MECHANISMS ASSOCIATED WITH DIGITAL ANOMALIES

By comparing the developmental underpinnings of digital development and anomalies, we speculate on the developmental pathways that may have been disrupted and produced those anomalies discovered in the cetacean manus. The majority of developmental studies typically use chick and mouse embryos to elucidate genetic mechanisms generating digital anomalies. In mice, the establishment of anterior–posterior patterning (digit number and identity) in tetrapod hands and feet is caused by the expression of Sonic Hedgehog (*Shh*) along the posterior mesenchyme of the limb bud (Hill, Heaney & Lettice, 2003; Tickle, 2006). Expression of *Shh* acts in a dose-

dependent manner to control growth, patterning, and morphogenesis of the manus (Schwabe & Mundlos, 2004; Tickle, 2006).

Polydactyly can be a result of disruption in anterior–posterior polarity of the manus, and this can be achieved via several mechanisms. Most commonly additional digit(s) lie along the anterior aspect of the manus (preaxial polydactyly) (Cohn & Bright, 1999; Lettice & Hill, 2005). Preaxial polydactyly can be experimentally generated by ectopically applying *Shh* to the anterior limb bud mesenchyme (Crick *et al.*, 2003; Schwabe & Mundlos, 2004; Tickle, 2006). Additional studies have documented that preaxial polydactyly is the result of point mutations in the limb-specific regulatory element of the *Shh* gene (Lettice & Hill, 2005). Similarly, mirror-image digit duplications are known to form as a result of applying *Shh* or *Shh*-expressing cells to the anterior margin of a chick wing (Crick *et al.*, 2003; Tickle, 2006). All extra cetacean digits and cases of polyphalangy reported here are expressed along the central digits, and are not mirror-image duplications of adjacent digits, leading us to speculate that the misexpression of *Shh* is probably not the mechanism driving cetacean digital malformations.

Cartilaginous interdigital elements (Fig. 3A), as first reported by Kükenthal (1893) and Burfield (1920), are now known to ossify in cetaceans, based on two specimens of *B. physalus* (Fig. 4C, D). Interdigital tissue has high chondrogenic potential, and chondrogenesis can be induced by several experimental methods, and in some cases, a novel digit can be created (Fig. 7; Sanz-Ezquerro & Tickle, 2003). A wound to the interdigital tissue during embryogenesis is sufficient to activate localized chondrogenesis, resulting in a novel digit (Talamillo *et al.*, 2005).

Branched digits, morphologically similar to those seen in *Tursiops* (Fig. 3E), *Delphinapterus* (Fig. 3F), and *Eschrichtius* (Fig. 4A, B), have been experimentally generated in model laboratory animals (Fig. 7). Researchers have formed branched digits by grafting a polarizing region from one chick limb bud to another (Sanz-Ezquerro & Tickle, 2003), or by adding bone morphogenic proteins (BMPs) to the anterior internal mesoderm (Fedak & Hall, 2004). Branched digits have also been found in human pathological cases. The rare human anomaly of synpolydactyly may display split metacarpals and duplicated phalanges joined by webbed skin (Goodman, 2002). Skeletal morphologies similar to human synpolydactyly are documented in rare specimens of *Eschrichtius* (Fig. 4A, B) and *Delphinapterus* (Fig. 3F, Yablokov, 1974). Human synpolydactyly is caused by a change in the *HoxD13* gene (the D cluster of homeobox genes on human chromosome 2). The *HoxD13* gene plays a role in controlling digit number (Talamillo *et al.*,

2005), and includes 15 alanine residues. However, in patients with synpolydactyly, the alanine residues are expanded, and as many as 25 alanine residues have been documented (Muragaki *et al.*, 1996; Goodman, 2002). The larger the expansion and number of subsequent alanine residues, the greater the portion of the digit was duplicated (Muragaki *et al.*, 1996; Goodman, 2002). The *HoxD13* gene of some specimens of *Delphinapterus* (Fig. 3F) presenting polyphalangy is predicted to have less of an alanine expansion than that of the *Eschrichtius* specimen (Fig. 4A, B) displaying polydactyly (Fig. 7).

Anomalous ossification of interphalangeal joints in some delphinid cetaceans can be explained by the activity of three genes essential for endochondral ossification: *Sox9*, Indian Hedgehog (*Ihh*), and *PTHrP*. Mechanical loading of the skeletal system can cause ossification, and even prechondrogenic mesenchyme cells can respond to compressive loads and increase cartilage production (Cohn & Bright, 1999). Chondrogenesis caused by external loading forces is regulated by *Sox9*, which directly activates the synthesis of collagen II (Cohn & Bright, 1999). Following the activation of the *Sox9* pathway, both *Ihh* and *PTHrP* are activated during endochondral ossification, and these genes can be expressed postnatally during bone ossification and fracture repair (Cohn & Bright, 1999). We therefore hypothesize that a possible explanation for delphinid phalangeal fusion could be the result of mechanical loading along the leading edge of joints, causing activation of the *Sox9* pathway, and resulting in localized ossification (Fig. 7). We hypothesize that this loading occurred postnatally while phalanges were undergoing endochondral ossification, and when the flipper was subjected to pressures generated by hydrodynamic flow.

CONCLUSION

This study surveyed cetacean forelimb radiographs and documented an abundance of various digital anomalies. Within odontocetes, approximately 11% showed a digital anomaly. Of those specimens with digital abnormalities, we most frequently observed element fusion in digits I and II. Also, accessory ossifications (polyphalangy and other centres of ossification) were observed more frequently than polydactyly (duplicated metacarpal). Several cases of exceptional joint ossification were documented in the dolphin *Steno*, as 25% of the sampled specimens displayed ossified joint edges, but the joint centres remained cartilaginous. Within mysticetes, this study documented the first record of mysticete polydactyly in a neonatal grey whale (*Eschrichtius*), and the first ossified elements in the interdigital spaces in some rorqual whales (*Balaenoptera*). Although this study is

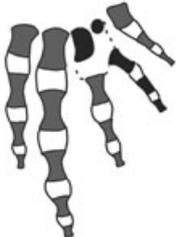
Digital Anomaly	Morphology	Possible Mechanism	Reference
Interdigital Polyphalangy	 <p>cartilaginous or ossified elements in interdigital space</p>	highly chondrogenic interdigital tissues	Sanz-Ezquerro and Tickle, 2003
Polyphalangy	 <p>duplicated phalanges, intact interdigital tissues</p>	slight expansion <i>HoxD13</i> gene alanine coding region	Muragaki et al., 1996; Goodman, 2002
Polydactyly	 <p>duplicated metacarpal (regardless of the number of additional phalanges), intact interdigital tissues</p>	greater expansion <i>HoxD13</i> gene alanine coding region	Muragaki et al., 1996; Goodman, 2002
Joint Fusion	 <p>ossified joints, fused elements</p>	upregulation of <i>Sox9</i> pathway	Cohn and Bright, 1999

Figure 7. Patterns of cetacean digital anomalies, and the possible developmental mechanisms that could generate these morphologies. Key: metacarpals, dark grey; phalanges, light grey; cartilages, white; anomalous elements, black.

limited to a basic morphological description, previously published studies have identified the genetic mechanisms causing abnormal digital ossifications. Based on these published data and on the morphology of digital anomalies reported here, cases of cetacean polyphalangy and polydactyly do not appear to be consistent with a misexpression of *Shh* (Hill *et al.*, 2003) or an *Shh* regulatory element (Lettice & Hill, 2005), but instead may be correlated with a change, specifically an alanine expansion, in the *HoxD13* gene.

Most mammals have digits that are separate from one another, but the interdigital webbing in the cetacean flipper masks any underlying skeletal anomaly,

and no superficial flipper morphologies are known to correlate with underlying digital anomalies. All of the digital anomalies cannot be seen in gross view as they lie in the plane of the flipper, and never protrude along the dorsal or palmar surfaces. Furthermore, digital anomalies are poorly studied, in that no evidence suggests if and how these anomalies affect flipper function. No study has tested whether cetacean flippers with extra or branched digits are in fact wider, although this widening has been documented in the developing limb buds of chicks and mice with experimentally induced polydactyly (Tickle, 2006). If cetacean flippers become widened so as to accommodate greater numbers of digits, this would

certainly affect flipper function, as the surface area and chord length would be increased, and therefore would directly change the hydrodynamic properties of the flipper. Furthermore, no evidence indicated whether these anomalous elements had any effect on the survival of the individual, but most radiographs were taken from stranded specimens. We also do not know the genetic catalyst for these digital anomalies, and whether they are pleiotropically linked with other potentially damaging or even fatal changes elsewhere in the body.

This study employed a small sample of cetacean forelimb radiographs and documented several anomalous ossifications, but future studies may offer insight by comparing the relative abundance of digital abnormalities between other groups of mammals, including those that also have flippers (e.g. pinnipeds and otariids). Furthermore, as other cetaceans bearing digital abnormalities strand, biopsies could be taken to identify the genetic underpinnings of these anomalies, as well as to explore the probable pleiotropic linkages between the genes associated with digital abnormalities and other anatomical abnormalities.

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