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Horses with solar foot penetration, deep digital flexor tendon injury, and absence of concurrent synovial sepsis can have a positive outcome

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Abstract
Solar foot penetration is one of the causes of deep digital flexor tendon injuries in horses, however, limited information is available on the prognosis for return to soundness in the absence of synovial sepsis. Objectives of this retrospective observational study were to describe low-field magnetic resonance imaging (MRI) findings and long-term outcome for a group of horses with this combination of clinical problems. Horses were included if low-field standing MRI of the foot was performed following puncture wounds, injury of the deep digital flexor tendon was diagnosed, and sepsis was confirmed to be absent in all adjacent synovial structures (distal interphalangeal joint, navicular bursa, and digital flexor tendon sheath). Medical records were reviewed and MRI studies were re-interpreted. Follow-up information was obtained via a telephone questionnaire at a minimum of 6 months post-injury. A total of 11 horses met inclusion criteria. In three horses, the deep digital flexor tendon injury was only visible in the T2 fast spin echo sequence and contrast radiography improved diagnostic certainty. The most commonly affected area was between the distal border of the distal sesamoid bone and the facies flexoria of the distal phalanx (6/11, 55%). Six horses (60%) had an excellent outcome (5, show jumping; 1, general purpose) and returned to full athletic function. Five horses (40%) were sound but had not yet resumed full work at the time of follow-up. Findings indicated that the prognosis for return to soundness can be good for horses with solar penetration, deep digital flexor injury, and absence of synovial sepsis.

KEYWORDS
deep digital flexor tendinopathy, equine, low field MRI, penetrating hoof injury, prognosis

1 | INTRODUCTION

Puncture wounds of the equine hoof are potentially serious injuries and are commonly diagnosed in equine practice. Although most solar penetrating injuries are superficial and have a good outcome with conservative treatment, deeper penetration of the foot, especially in the frog (cuneus ungulae) and the collateral sulci may have a much graver prognosis and can represent a life-threatening or performance limiting injury for the horse. Deep structures that may be damaged during foot penetration include the deep digital flexor tendon, distal phalanx, ungular cartilages, digital cushion, bursa podotrochlearis (navicular bursa), distal sesamoid bone, digital flexor tendon sheath, distal interphalangeal joint, and distal sesamoidean impar ligament. Early determination of the structures involved combined with prompt appropriate treatment is considered central to achieving a successful outcome.

Conventional imaging modalities, including radiography, diagnostic ultrasonography, and nuclear scintigraphy, have significant limitations when evaluating the structures within the foot. Magnetic resonance Imaging (MRI), alternatively, can provide three-dimensional evaluations of the foot, providing information on both osseous and soft tissue structures. Magnetic resonance imaging features following acute or chronic penetrating injuries have been described and two case reports have demonstrated the potential prognostic value, although only small numbers of horses were reviewed.
The reported postsurgical successful rate for return to previous athletic function after solar foot penetration ranged from 30% to 63% and the majority of the studies have looked more specifically at synovial sepsis following foot penetration. Although a high proportion of the described cases in all published reports had a traumatic lesion in the deep digital flexor tendon, the outcome of horses recovering from penetrating injury where synovial sepsis has been excluded has not been investigated to the authors’ knowledge.

The objectives of this study were to describe low-field MRI findings, treatment approaches, and long-term outcome for a group of horses with solar penetration, deep digital flexor tendon injury, and absence of synovial sepsis.

### 2 | MATERIALS AND METHODS

All owners of horses included in this retrospective observational study had signed an owner informed written consent form that was approved by the University of Edinburgh Human Research Ethical Review Committee. Sample size was based on the available cases that fit inclusion criteria during the study period. Computerized and hardcopy medical records of horses that had incurred puncture wounds through the foot and that were admitted to the Equine Hospital of The Royal (Dick) School of Veterinary Studies of Edinburgh between May 2010 and July 2016 were reviewed. Horses were selected for inclusion in the study if low-field standing MRI of the foot was performed following puncture wounds, injury of the deep digital flexor tendon occurred, and sepsis was confirmed to be absent in all adjacent synovial structures (distal interphalangeal joint, navicular bursa, and digital flexor tendon sheath). Cases were excluded if synovial fluid was not collected or if insufficient volume of synovial fluid was available for analysis. Synovial fluid exclusion parameters were based on identification of any of the following: total nucleated cell count > 20 x 10⁶ cells/L, >90% neutrophils in a manual smear, or total protein concentration > 30 g/L. Selection of site for synoviocentesis was at the attending clinician’s discretion but included one or more of the following structures: navicular bursa, digital flexor tendon sheath, and distal interphalangeal joint. Subject inclusion or exclusion decisions were made by an intern (S.S.), under the supervision of board-certified veterinary surgeons (S.T., Y.E.) and a board-certified veterinary radiologist (T.S.).

The same intern recorded the following data based on medical record entries: patient signalment, duration of time from injury to hospital admission, foot affected, location of the solar penetration, concurrent soft tissue injuries, and treatments administered prior to admission. Horses that had MRI evaluation within 21 days of injury were described as acute cases and horses that had an MRI evaluation more than 21 days post-injury were described as chronic. Performance disciplines were categorized as eventing, show jumping, dressage, racing, or general purpose. Horses competing at an unaffiliated level were categorized as eventing, or general purpose. Horses competing at an unaffiliated level were described as acute cases and horses that had an MRI evaluation more than 21 days post-injury were described as chronic. Performance disciplines were categorized as eventing, show jumping, dressage, racing, or general purpose. Horses competing at an unaffiliated level were assigned to the general-purpose group. Lameness was graded by board-certified veterinary surgeons (S.T., Y.E.) at the time of hospital admission, using a previously published lameness scoring method (0 = sound, 10 = non-weight bearing).

As part of the inclusion criteria, low-field MRI was performed using the same protocol in all horses. Horses were sedated and scanned in a standing position using a 0.27 Tesla open magnet and dedicated extremity radio frequency coil (Hallmarq Veterinary Imaging Ltd, Guildford, Surrey UK). Images were acquired in sagittal, transverse (including perpendicular to the deep digital flexor tendon at all examined levels), and dorsal planes using T1-weighted high resolution and gradient echo high resolution; T2*-weighted three-dimensional, gradient echo, and fast spin echo (FSE); T2-weighted and FSE short tau inversion recovery sequences (Table 1). Archived magnetic resonance images were retrieved and re-interpreted by board-certified veterinary surgeons (S.T., Y.E.) and a board-certified veterinary radiologist (T.S.), using dedicated diagnostic imaging viewing software (Osirix DICOM viewer, Osirix-Pixmeo SARL, Bernex, Switzerland; www.osirix-viewer.com). In an effort to control bias, readers for the MRI studies were blinded to case history and clinical details at the time of interpretation. Any differences in interpretations were later resolved based on a consensus for further analyses.

Long-term follow-up was obtained via a telephone questionnaire conducted with the referring veterinarians, owners, or trainers. Questionnaires included information about further treatment required following discharge, the level of soundness achieved, and return to athletic function at the level prior to injury. The outcomes were categorized as excellent (horse returned to previous athletic function without recurrent lameness), moderate (sound but light work only), or poor (still lame or humanely destroyed due to persistent lameness). Horses that had an excellent or a moderate outcome when classed together were described as paddock sound. Outcome data were recorded by the first author (S.S.) via telephone questionnaire, these data were then collated by the first and senior author (a board-certified veterinary surgeon; S.S.). Descriptive analyses of data were carried out by an imaging intern (Microsoft Excel for Mac 2011, Microsoft, version 14.6.7).

### 3 | RESULTS

#### 3.1 | Descriptive data

A total of 692 horses had MRI examinations during the study period and 24 of these horses (3.5%) had solar penetrations. A total of 11 horses met all required inclusion criteria for the study. Seven (64%) were male and four (36%) were female. Represented breeds were as follows: Warmblood (n = 5), Thoroughbred (n = 2), cob (n = 1), draught breed (n = 1), Appaloosa (n = 1), and Connemara Pony (n = 1). The median age was 11 years, with a range of 4–18 years. The majority of cases were used for show jumping (n = 5), dressage (n = 1), hunting (n = 1), or flat racing (n = 1). The rest of the cases (n = 3) were pleasure horses and assigned to the general-purpose group. Forelimb and hindlimbs were affected with similar frequency, with five of the injuries occurred in forelimbs and six in hindlimbs. The mean time from injury to the presentation at the Equine Hospital of the Royal (Dick) School of the Veterinary Sciences was 38 days (range 1 day to 6 months). Four cases were presented for MRI due to recurring lameness following chronic penetrating foot wounds; in these horses the average time
from injury to MRI scan was respectively 30 (n = 2), 42, and 60 days. Synovial sepsis was excluded in four cases (n = 4) by the referring veterinary practices at the time the penetrating injuries occurred and in seven (n = 7), once the patient was admitted at the referral hospital. Synoviocentesis and fluid analysis of the digital flexor tendon sheath was performed in four cases (n = 4), of the distal interphalangeal joint in four (n = 4), analysis of both the digital flexor tendon sheath and distal interphalangeal joint in one (n = 1), and both the distal interphalangeal joint and navicular bursa in two (n = 2).

Digital radiography (AGFA CR MD 4.0 General imaging plate, Agfa HealthCare NV, Seppestraat 27, B-2640, Morstel, Belgium) was used to aid and support diagnosis in nine horses (n = 9). A sterile blunt probe was also used to identify the depth and direction of the tract in four cases (n = 4). Radiographic projections routinely obtained were lateromedial (63 kV 10 mAs), dorsopalmar/plantar (63 kV 10 mAs) and dorsoproximal-palmaro/plantarodistal oblique (63 kV 6 mAs). In acute cases, contrast radiography of the navicular bursa, digital flexor tendon sheath, and distal interphalangeal joint was used to determine communication between these synovial structures and the tract, this was normally carried out following MRI examinations. Arthrography and bursography were performed immediately after injecting a 1:1 ratio of 0.9% saline: Iohexol (Omnipaque™ GE Healthcare AS, Nycoveien 1-2, NO-0401, Oslo, Norway). Contrast medium and volumes injected varied from 2 to 10 mL, depending on the size of the joint concerned.

The type of foreign body was unknown in five horses, a piece of wood in a single case and a nail or a metal wire in the majority of the cases (n = 5). The exact location of the penetration was into the central sulcus of the frog, including the medial or lateral collateral sulci, in nine horses (n = 9), following by the palmar/plantar area in two cases (n = 2). The median grade of lameness on presentation was eight of 10 at 10

The median time of hospitalization in all horses was 8 days (range 1 day to 1 month). Treatment at the time of admission and hospitalization included superficial paring out of the tract, aseptic preparation of the foot, bandaging with a sterile dressing, and parenteral administration of broad-spectrum antimicrobial and, in some cases, oral or parental administration of anti-inflammatory drugs. Six horses also received one or more antimicrobial limb perfusions intravenously in the affected leg. The antimicrobial of choice for perfusion was either Amikacin (500 mg diluted in 60 mL lactated Ringer’s solution) or Gentamicin (1 g in 60 mL sterile normal saline solution). Surgical exploration was performed in two horses with a greater degree of lameness than anticipated from the injuries identified during the clinical examination and MRI scans. In two cases, pedal bone osteitis was the main finding during surgery, and both horses made an excellent recovery. Euthanasia occurred for one horse due to the severity of lesions seen on magnetic resonance images, persistency of severe degree of lameness during hospitalization, and financial constraints of the owner.

### 3.2 Magnetic resonance imaging findings

Penetrating tracts were visible as focal areas of a reduced signal in all MRI scans, based on reader consensus. Differentials for the signal voids were gas accumulation, mineralization, or deposit of hemosiderin. The T1-weighted and T2*-weighted images showed a clear signal void tract in all horses (n = 7) with an acute history of penetrating injury. Isolated signal void focal areas were observed in chronic cases (n = 4) presented for persistent or recurrent lameness following solar foot penetration (Figure 1). The most commonly (n = 6) affected area was between the distal border of the distal sesamoid bone and the facies flexoria of the distal phalanx. In two cases the penetration occurred at the level of the palmar/plantar digital cushion. In the remaining horses (n = 3), the area involved was from the distal border of the distal sesamoid bone and proximal recess of the navicular bursa. Involvement of the deep digital flexor tendon was identified in all MRI scans. In three cases where deep digital flexor tendon injury was suspected, signal void in the gradient echo sequences partially obscured the tendon and surrounding structures. Interpretation of deep digital flexor tendon involvement was therefore reliant on T2 FSE sequences in these cases (Figure 2). Digital radiography and the use of a sterile blunt probe were considered by readers to be particularly helpful for supporting MRI questionable diagnoses of deep digital flexor tendon injury. Magnetic resonance imaging characteristics of deep digital flexor tendon injury and concurrent structure involvement for each individual case are provided in Supporting Information 1. Involvement of the distal phalanx was seen as hyperintense signal on T2 and short tau inversion recovery sequences and was identified in seven cases (Figure 3). A metal foreign body was suspected in case 7 (Figure 4).

### 3.3 Outcome

All 11 horses were discharged from the hospital, and follow-up information was available for all of them. All cases received box/small padock rest and controlled walking exercise for up to 1 h/d, for a minimum of 1 month. Corrective trimming and shoeing, consisting of 5–7-degree heel wedge shoes with good palmar heel support, was performed in all cases for at least two shoeing cycles (every 4–6 weeks).
All horses returned to soundness, and all their owners/trainers were satisfied with their horses’ outcome. Six horses (60%) had an excellent outcome (five show jumping; one general purpose) and returned to full athletic function; a further five (40%) were sound but had not yet resumed full work at the time of writing. The median time to return to full work was 6 months (range 1 month to 1 year) for horses that had an excellent outcome and 8 months (range 6 months to 1 year) for horses that were paddock sound at the time of follow-up. Two horses were subjected to euthanasia for causes not related to lameness; however, both had returned to soundness at the time euthanasia was performed.

4 | DISCUSSION

Findings from the current study indicated that horses can have a good outcome and return to athletic function after sustaining a solar penetration involving the deep digital flexor tendon, in the absence of synovial sepsis. This prognostic information can be helpful for veterinarians and clients. In the present study, plain radiography, radiography with a sterile metal probe placed in the tract, and contrast radiography were techniques used to assess the direction and depth of the penetration tract, and to investigate the involvement of vital structures (primarily synovial structures). Although it was possible in a few cases to predict involvement of the deep digital flexor tendon by assessing the distance between the end of the metal probe and the flexor surface of the navicular bone, these techniques could not conclusively identify deep digital flexor tendon damage in cases where the penetrating tract was no longer accessible. Transcuneal or distal pastern ultrasonography was not performed. Scans performed via the sagittal midline of the frog might have had diagnostic value, as the majority of the horses in the present study had severe tendinopathy in the insertion of the deep digital flexor tendon on the distal phalanx. However, lesions occurring at the level of the navicular bone will be seen by ultrasonography only if they lie in the midline. Therefore, lesions confined to either the medial or lateral part of the deep digital flexor tendon, would not have been visible, nor would the extent of the bony changes.

Nuclear scintigraphy could also have been used to yield additional information. Boado et al. reported a correlation between nuclear scintigraphic and MRI findings in two horses with a history of unresolved lameness due to chronic solar penetrating injuries. However, false negative scintigraphic abnormalities have been reported in horses with MRI evidence of tendonitis of the deep digital flexor tendon, but generally in horses with the lameness of more than 3 months’ duration.

The potential value of MRI for the diagnosis and identification of affected structures in solar penetrating injuries of the foot has been reviewed in two previous case series. Kinns and Mair described three cases that were imaged 48 h to 6 weeks after initial injury. All cases had deep digital flexor tendon pathology confirmed on MRI, and synovial sepsis was excluded. All horses returned to soundness 3–11 months after injury with a variable time of box-paddock rest. A further case series reported the MRI findings in two horses with chronic forelimb lameness. A penetrating tract and a lesion within the deep digital flexor tendon were identified on high field MRI examination in both horses. Based on the severity of the injuries and the chronicity of the lameness, both animals were subjected to euthanasia. Both studies supported the prognostic value of MRI in assessing solar penetration injuries, suggesting that MRI should be used to accurately identify deep digital flexor tendon lesion following penetrating injuries and is a help-
ful aid in deciding the most appropriate treatment (eg, medical therapy, surgical therapy, and therapeutic shoeing) and determining the prognosis. However, only small numbers of horses were reviewed in these studies. A larger scale retrospective study evaluated the imaging findings in 55 horses that underwent standing low-field MRI examination following solar penetration. In total, 37 of the 55 cases had deep digital flexor tendon damage; no data regarding long-term outcome was obtained. In the same study, the main factors affecting the prognosis were identified in the area and structure involved in the penetrating injury, with 65% of the animals undergoing euthanasia having a lesion in the region between deep digital flexor tendon insertion on the distal phalanx and its palmaroproximal aspect. Of all animals undergoing euthanasia, 85% had a lesion involving the deep digital flexor tendon. However, no information was given regarding the presence or absence of synovial sepsis and whether this could be the factor influencing prognosis. Nonetheless, MRI diagnostic and prognostic values were endorsed. More recently a review article discussed if MRI should be used to evaluate horses presented for penetrating injuries of the foot. In this previous paper, the author concluded that MRI was useful in the assessment of tract direction and depth, and evaluation of soft tissue injuries. The authors also suggested a combined approach using MRI and radiography and synoviocentesis, when necessary, to best assist clinicians with therapeutic approach and prognostication.

In the present study, readers considered MRI to be helpful for evaluating the extent of the tract, assessing concurrent soft tissue and osseous injuries, and detecting potential involvement of synovial structures (navicular bursa, digital flexor tendon sheath, and distal interphalangeal joint joint). Contrast radiography and synovial fluid analysis were considered to be supportive techniques for excluding communication and sepsis of the synovial structures affected by the penetrating injury.

Involvement of the deep digital flexor tendon was identified in all MRI scans. However, the main limitation we experienced was the ambiguous interpretation of deep digital flexor tendon lesions in three cases. Variable size signal void areas partially obscured the tendon margins and surrounding structures. These areas of hypointense signal recognized in association with the penetrating tract were more severe on gradient-echo than spin-echo sequences and could possibly be explained as a manifestation of mineralization, gas accumulation, deposits of hemosiderin, or metal susceptibility artifacts. It is indeed expected that foreign bodies, such as metal wires or nails, may release metal debris while penetrating within the foot and create significant magnetic field inhomogeneities artifacts around them.

Furthermore, deep digital flexor tendon lesions detected on MRI in this study differed from most commonly reported strain-type injuries of the deep digital flexor tendon. These injuries have been previously categorized into the following four types: core, dorsal border, sagittal plane split, and insertional injuries. In the horses described here, the primary lesions were near the focal areas of hypointense signal and extended through the deep digital flexor tendon and the peritendinous soft tissue. Although the MRI signal abnormalities of the deep digital flexor tendon can be similar between horses with and without a history of penetrating injury, marked differences in the peritendinous soft tissue MRI appearance can differentiate between overstrain injury and acute trauma due to a penetrating foreign body.
Dyson et al. described the outcome of conservatively managed deep digital flexor tendon injuries, as part of a larger group of horses with foot pain. Animals received box rest and controlled walking exercise for up to 1 h/d, for a minimum of 6 months. Corrective trimming and shoeing were performed on an individual basis. Thirteen of 47 (28%) horses with primary deep digital flexor tendon injuries and long-term follow-up returned to full function; 19% were sound but had not resumed full work while 53% had persistent or recurrent lameness. The prognosis was worse for horses with combined navicular bone and deep digital flexor tendon injuries. Only three of the horses included in the study had MRI evidence of a previous puncture wound, but no specific follow-up information was presented, and neither were investigated possible features of variation in their prognosis concerning lesion type and location.

Previous publications have recognized the site of the penetrating injury as one of the principal factors affecting the prognosis. In the present study, the most commonly (n = 6) affected area was between the distal border of the distal sesamoid bone distal to the facies flexoria of distal phalanx. In two cases, the location of the penetration occurred at the level of the palmar/plantar region (from the palmaro/plantaroproximal aspect of the distal phalanx to the heel) of the foot. In the remaining horses (n = 3) the area involved was the central frog region, from the distal border of the distal sesamoid bone and proximal recess of the navicular bursa. Case 5 (Figures 1 and 3) illustrated the potential usefulness of MRI for horses with a solar injury that continue to show mild to moderate lameness 3 weeks post injury.

Varying degrees of treatment success have been reported following solar foot penetrations, and the majority of the studies have looked more specifically at synovial sepsis following foot penetration. Kilcoyne et al. reported an approximately 60% return to soundness following solar foot penetration involving the frog and lateral or medial collateral sulci in 63 horses. Of these 63 horses, 20 had involvement of the superficial corium and digital cushion and only nine had a solar penetration and concurrent involvement of the distal phalanx without...
synovial sepsis. A good prognosis (88%) was also reported for those cases involving the distal phalanx (n = 9). In the same study, a poor outcome (29%) was reported for those cases with penetration of a synovial structure (n = 34). However, the outcome of horses with a primary injury of the deep digital flexor tendon was not described and MRI examination was not performed. Two studies reported treatment following the ‘street nail’ procedure, in which radical excision of the penetrating tract and resection or fenestration of the deep digital flexor tendon was performed. These studies reported a return to soundness for either breeding or riding of approximately 30%. Furthermore, the street nail procedure has been widely superseded by endoscopic lavage of the navicular bursa and other synovial structures, which provides improved visualization and more thorough lavage. In the same study, a good outcome (75%) and return to soundness was reported for horses (n = 16) with contaminated or septic navicular bursae and 63% of them returned to the previous level of athletic function. A large retrospective study evaluated the outcome for 95 horses with solar penetration wounds that underwent surgery for synovial sepsis. Findley et al. stated that the majority of horses sustained injuries to three structures, most commonly deep digital flexor tendon, distal interphalangeal joint, and navicular bursa. It was not reported how the deep digital flexor tendon injuries were confirmed and only 31 horses in this study underwent MRI; the findings of the MRI examination are not described. These authors have reported a 36% return to pre-injury athletic function with a hospitalization survival rate of 56% (n = 95).

Although a high proportion of the described cases in all published reports had a traumatic lesion in the deep digital flexor tendon outcome of horses recovering from penetrating injury where synovial sepsis is not a concern has never been investigated in a reasonable number of horses. Hence, the need to provide information and guidance for owners and veterinary surgeons for cases with such injuries. The outcome of horses that met the inclusion criteria (exclusion of synovial sepsis and MRI identification of deep digital flexor tendon trauma following a solar penetration) was good–excellent. In fact, of the 10 horses discharged from the hospital, all returned to soundness, and the majority of them (n = 6) returned to full athletic function. The average time to return to full work was approximately 6 months (range 1 month to 1 year) for horses that had an excellent outcome (n = 6) and about 8 months (range 6 months to 1 year) for horses (n = 4) that were sound at the time of follow-up.

Susceptibility artifacts post fetlock arthroscopy have been reported in 40% of cases. The cause of these artefacts was reported as hemosiderin or microscopic metallic material both of which could cause susceptibility artifacts following solar penetration. Hypointense (T1, T2*, and T2 FSE) susceptibility artefacts were identified in the two cases that had MRI evaluation within 1 day of penetrating injury suggesting that microscopic metallic fragments may be a cause as hemorrhage should be isointense on T1 scans within this time frame. Of the remaining five acute cases scanned at 10–21 days post-injury, two had hypointense susceptibility artefacts that were scanned at 10 days and 15 days post-injury consistent with the presence of hemosiderin. In such low numbers of cases it is not possible to determine the most appropriate time frame post-injury when an MRI examination should be performed. Repeat MRI of case 7 (Figure 4) at 6 and 12 months post-injury demonstrated the same circular susceptibility artifact.

There are some limitations of the current study that are common to all retrospective studies, such as missing data and selection bias. Only horses referred to the Dick Vet Equine Hospital were included; however, a proportion of animals with a perceived poor prognosis following solar foot penetration may have been subjected to euthanasia.
before referral or following evaluation at the referral center without undergoing MRI examination.

In conclusion, the current study supported findings from previous studies indicating that deep digital flexor tendon traumatic injury is a possible sequela of solar foot penetration and that horses can return to full athletic performance if there is an absence of synovial sepsis. In addition, the current study supported the use of low field MRI as a method for characterizing the extent of penetrating tracts, detecting deep digital flexor tendon injuries, and assessing involvement of adjacent soft tissue structures.

**LIST OF AUTHOR CONTRIBUTIONS**

**Category 1**

(a) Conception and Design: Cillán-García E, Taylor SE
(b) Acquisition of Data: Schiavo S, Elce Y, Liuti T
(c) Analysis and Interpretation of Data: Taylor SE, Schiavo S, Elce Y, Liuti T

**Category 2**

(a) Drafting the Article: Schiavo S
(b) Revising Article for Intellectual Content: Taylor SE, Cillán-García E, Liuti T, Elce Y

**Category 3**

(a) Final Approval of the Completed Article: Schiavo S, Taylor SE, Cillán-García E, Liuti T, Elce Y

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**SUPPORTING INFORMATION**

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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