Through a Scanner Darkly

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The recent paper by Lee, Lai, Brodale, and Jampolsky in IOVS claims absence of rectus extraocular muscle (EOM) pulleys in humans.[1] Readers will naturally wonder how these authors can make a claim contradicting two decades of persuasive scientific evidence. The explanation lies in both methodological and technical errors, as well as in the paradigm embraced by the Jampolsky laboratory. The errors may be grouped into four types.

<u>Error 1. Misunderstanding of Ocular Kinematics.</u> Lee et al. misunderstand Listing's Law (LL), which states that with the head upright and stationary, any secondary or tertiary eye position can be reached by rotation from a primary position about a single position axis, and that all possible position axes of the eye lie in a single plane, Listing's plane (LP).[2] Lee et al. failed to appreciate the crucial fact that the three-dimensional (3-D) eye velocity axis differs from the position axis.[3] Tweed demonstrated that in the position domain, LL is mathematically equivalent to changing the 3-D ocular velocity axis by half of eye position.[4] In Lee et al.'s "model" of EOM paths in their Figure 1, the position axis for vertical eye movements was incorrectly assumed to shift by half of horizontal eye position. The shifts in ocular position axis illustrated in Lee et al.'s Figure 1 would permit only axes lying in a grossly non-physiological horizontal plane. A valid position axis for supraducted adduction in a physiologic LP would have to lie in something approximating the frontoparallel plane, but angled from inferonasal to superotemporal. Thus, Lee et al. have arbitrarily assumed rotational axes violating LL for modeling their data.

Lee et al.'s Figure 1B models medial rectus paths in the presence of pulleys rigidly-fixed in the orbit. This is a straw-man comparison, since no one believes that the orbitally-stabilized pulleys assumed in Figure 1B could implement LL,[5] and the pulleys were always supposed to have soft, elastic suspensions capable of small deformations. Instead, in 2000 the active pulley hypothesis (APH) proposed that pulleys shift anteroposteriorly so that each EOM's pulling direction changes by half of eye position to implement LL.[6] A large body of quantitative MRI data has since accumulated to support the APH (detailed reviews[5,7-11] summarize primary publications). Lee et al.'s comparison of observed vs. model data is invalid, as they compared their path model with an old pulley model not supposed to implement LL mechanically.

Lee et al. offer as an alternative the "restrained shortest-path model," an oxymoron analogous to mixing oil with water. Their Figure 6 actually uses the inaccurate label "shortest path model" to depict sideslip limited to 2.5 mm.1 A true shortest path assumption would require medial rectus sideslip exceeding 8 mm for the gaze positions studied by Lee et al., rather than the 0.2 – 1. 5 mm mean values they reported. Robinson[12] and Miller and Robinson[13] assumed constraint on rectus EOM sideslip because computational models assuming a shortest (great circle) path were inconsistent with any eye position except for flipping of the cornea back toward the orbital apex. Miller and Robinson were careful to distinguish the constrained path assumption that limited EOM sideslip, from the shortest path hypothesis that permitted sideslip freely, but these modeling pioneers acknowledged that they had merely guessed the constraints in order to implement workable computer models.[12,13] Assumption of any constraints on EOM sideslip already defeats the shortest path hypothesis as portrayed by Lee et al.

Error 2. Inadequate Imaging Technique. While criticizing imaging studies from the 1980's for low resolution, Lee et al. claim superior imaging technique.[1] In fact, the MRI resolution of Lee et al. is inferior to that employed by most investigators since the early 1990's. Lee et al. imaged axially, and reformatted into coronal and sagittal planes, with rotational and translational shifting to compensate for head motion. Reformatting alone reduced Lee et al.'s in-plane resolution to the diagonal of the primary image plane voxel, in this case 0.705 mm. Additional resolution loss due to rotational and translational effects of head motion also explain the blurriness of the images published by Lee et al. in their Figures 2 – 4. By comparison, data at in-plane resolution 0.312 mm or better support the existence of pulleys.14,15 Lee et al. did not specify how they determined EOM positions from their images, but their figures suggest use of gross estimation from EOM borders in sagittal reconstructions. Such technique is susceptible to partial volume averaging and slight changes in EOM shape, and has a resolution no better than ±1 pixel (0.7 mm in Lee et al.'s case). Miller first proposed that EOM centroids in transverse planes represent the best measure of path,16 because centroids reflect EOM force direction and can be determined more precisely at subpixel resolution. Until Lee et al., all subsequent quantitative MRI of the EOMs has employed Miller's rigorous technique.

Error 3. Reported Data Do Not Support Claims. The average medial rectus sideslip claimed by Lee et al. is 0.2 - 1.5 mm, which is only 66% of the prediction of their flawed geometrical model and a tiny fraction of the more than 8 mm anticipated from the shortest path hypothesis. Some of the subjects studied by Lee et al. exhibited zero to 1.0 mm sideslip over the range of 70° horizontal and 60° vertical eye movements. Even at face value, Lee et al.'s findings hardly refute the idea of constraint on EOM sideslip. Although Lee et al. claim to have found gradual changes in EOM path, the sagittal images in their Figure 2A show parallel offsets in the entire medial rectus path that would have required implausible sideslip even at the annulus of Zinn. Such a result is not only incompatible with the model in their Figure 1A, but also easily explained as an artifact of image translation or its correction by the SPM2 software.

Lee et al. were emphatic of the negative finding that their sagittal images showed no medial rectus path inflections. That negative result could constitute evidence only if Lee et al.'s low resolution MRIs were capable of resolving inflections. Superior MRI technique has demonstrated clear inflections in paths of all four human rectus EOMs in secondary[14] and tertiary gazes,[15] quantitatively consistent with the APH. Moreover, in eccentric vertical gaze, the lateral rectus path shifts slightly in a direction opposite the prediction of the shortest path hypothesis.[14] It is notable that the images collected by Lee et al. should also have permitted analysis of the paths of the superior, lateral, and inferior rectus EOMs. Is it possible that this data was not presented because these EOMs do not exhibit sideslip consistent with the notions of Lee et al? Lee et al. did not even claim any appreciable sideslip except for the medial rectus in abduction. It seems insufficient to challenge the existence of pulleys based on an isolated observation for only the medial rectus in abduction, particularly if this observation were inconsistent with the behavior of the other three EOMs and for other gaze directions. Lee et al. should publish their data for the other EOMs.

Error 4. Discussion Emphasizes Abandoned Theories. Lee et al.'s discussion ignores long-recognized findings contradicting their conclusion, while repeating alternative hypotheses now abandoned by even their authors. For example, Lee et al. propose that rectus EOM sideslip may be limited by musculo-global tissue connections, an idea assumed by Miller and Robinson as the possible anatomic basis for restricted sideslip,[13] and plausible until 1993. In that year, high resolution MRI scans before and shortly after large transpositions of rectus EOM insertions demonstrated continued EOM path stability and the presence of path inflections.[17] Since pulley effects persisted after all musculo-global tissue connections had been severed by surgery, it is untenable to maintain, as do Lee et al., that such connections could provide rectus path stability.

Lee et al.'s presentation of the electrophysiology literature is inaccurate. They avidly cited Angelaki and Hess's early skepticism that pulleys, rather than explicit neural commands, could be the basis of LL.[18] However, Lee et al. then went on to dismiss as conceptually misguided the elegant experiments later performed in the Angelaki lab in behaving monkeys that have decisively settled this issue in favor of mechanical, rather than neural, factors. First, electrical stimulation of the abducens nerve evokes eye movements conforming to LL, absent any other changes in EOM innervation patterns.[19] That implies that LL must be mechanically implemented. Second, direct recordings from the motoneurons that innervate all of the vertical rectus and oblique EOMs failed to demonstrate the torsional signal for LL that would be required if LL were neurally specified.[20] Finally, Lee et al. ignore high resolution MRI evidence indicating that the oblique EOMs reposition the rectus pulleys to implement eye movements not conforming to LL, such as convergence[21] and the vestibulo-ocular reflex.[22] In their discussion, Lee et al. inaccurately denied that the APH allows for the pulley shifts we have described in the foregoing detail.

Why Do Lee et al. Ignore the Evidence? The reader may be perplexed by the Jampolsky lab's denial of voluminous evidence that other scientists find compelling. Pulley action on EOMs was first proposed in 1989 by Joel M. Miller.[16] The noted philosopher of science, Thomas Kuhn,[23] has provided an explanation of Lee et al's behavior. Dr. Jampolsky and his colleagues are adherents to a traditional paradigm of EOM function built on the basis of strabismus surgical experience. This traditional paradigm is a self-contained approach to conceptualizing EOM actions, but beset by internal and external inconsistencies, and largely unvalidated against other sources of evidence. Over the last two decades, Joel Miller initiated a different paradigm of the EOMs and connective tissues that is consistent with considerable external evidence. Dr. Jampolsky and colleagues reject that modern paradigm.

Thomas Kuhn has explained that the development of a novel paradigm represents a "scientific revolution."[23] So many concepts change in a scientific revolution that adherents to the old and new paradigms find communication impossible, and cannot agree on mutually acceptable evidence. Kuhn has explained that this mis-communication arises because paradigms constrain the sort of observations that might be considered "evidence" in the first place.

Thomas Kuhn has provided historical examples illustrating times of scientific revolutions, when competing paradigms briefly coexisted.23 Kuhn showed that competing scientific paradigms cannot coexist indefinitely. Eventually, new paradigms prevail if they offer advantages to practitioners of science, including better and more elegant abilities to explain existing observations, internal consistency, and the capacity to predict novel observations. A new paradigm ultimately succeeds if it is more useful than the older paradigm. It is anticipated that students of orbital and EOM anatomy, ocular motility and the neurosciences, as well as clinicians interested in the correction of strabismus, will find the concept of pulleys useful to them.

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