Magnetic resonance imaging-based measurement of internal deformation of vibrating vocal fold models

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A method is presented for tracking the internal deformation of self-oscillating vocal fold models using magnetic resonance imaging (MRI). Silicone models scaled to four times life-size to lower the flow-induced vibration frequency were embedded with fiducial markers in a coronal plane. Candidate marker materials were tested using static specimens, and two materials, cupric sulfate and glass, were chosen for testing in the vibrating vocal fold models. The vibrating models were imaged using a gated MRI protocol wherein MRI acquisition was triggered using the subglottal pressure signal. Two-dimensional image slices at different phases during self-oscillation were captured, and in each phase the fiducial markers were clearly visible. The process was also demonstrated using a three-dimensional scan at two phases. The benefit of averaging to increase signal-to-noise ratio was explored. The results demonstrate the ability to use MRI to acquire quantitative deformation data that could be used, for example, to validate computational models of flow-induced vocal fold vibration and quantify deformation fields encountered by cells in bioreactor studies. © 2019 Acoustical Society of America. <https://doi.org/10.1121/1.5091009>

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I. INTRODUCTION

During phonation the vocal folds undergo high frequency vibration, relatively large amplitudes and strains, and repeated collisions, leading to complex vocal fold (VF) tissue deformation, strain, and stress responses. The same can be said for VF models used in voice research studies. For diagnosis and research purposes, the vibrating surfaces of VFs and VF models can be at least partially directly observed via clinical endoscopy (*in vivo*) and other imaging methods (*ex vivo* and *in vitro*). Less accessible are interior regions. However, being able to quantify the internal stress and strain fields during vibration is important because mechanical stimuli play key roles in tissue development, mechanical properties, and pathogenesis (Titze, 1994; Titze *et al.*, 2004; Gaston *et al.*, 2012; Latifi *et al.*, 2016). Thus the ability to experimentally measure internal deformation could benefit voice modeling and tissue engineering research. The purpose of this paper is to demonstrate, using scaled-up self-oscillating VF models, the potential for use of magnetic resonance imaging (MRI) as a tool to acquire such data.

Deformation and resulting stress experienced by VFs during vibration have been predicted by mathematical and computational models. These include, for example, a mathematical model based on simple physical assumptions to estimate stress experienced by the VFs (Titze, 1994) and finite element models to study VF stress (Jiang *et al.*, 1998;

Gunter, 2003, 2004; Tao and Jiang, 2007). To maximize the potential benefit of computational models such as these, validation is required. Model validation may be accomplished via quantitative comparison with human voice data, such as onset pressure, frequency, and glottal width amplitude, or via comparison with complementary laboratory model data. For example, Bhattacharya and Siegmund (2014) used the comparison of the pressure and displacement results from synthetic VF models to validate a computational fluid dynamics model. Validation is particularly important in the development of high-fidelity models intended for clinical application, and validation of individual-specific vibratory characteristics has been cited as one of the major challenges facing development of patient-specific models (Chang *et al.*, 2016). While quantitative data such as onset pressure, frequency, and glottal width can be readily obtained for validation purposes, internal deformation, strain, and stress are quantities that have largely eluded validation due to technological challenges.

Measurements of internal VF deformation, strain, and stress during vibration are also needed for purposes other than validation. Quantitative descriptions of these variables can yield insight into VF mechanobiology via bioreactors in which biomaterials are subjected to a phonomimetic mechanical environment to quantify the effects of stress and strain on VF tissue. For example, to better understand how VF vibration affects the extracellular matrix (ECM), Titze *et al.* (2004) created a bioreactor that subjected cell-seeded scaffolds inside a cell culture flask to vibratory stimuli at similar frequencies and amplitudes that VF cells experience

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in vivo. Similarly, Gaston *et al.* (2012) applied stress to cell scaffolds in a sinusoidal pattern to mimic the mucosal wave and Latifi *et al.* (2016) embedded cell scaffolds into synthetic, self-oscillating VFs.

While measuring internal deformation is important for VF model validation and other applications, measuring these quantities is not trivial. Limited optical access precludes many methods and embedded sensors are intrusive. Medical imaging presents a possible approach, such as the use of ultrasound and digital image correlation via speckle-tracking echocardiography to study the vibratory behavior of the VFs *in vivo* (Tsai *et al.*, 2009).

The purpose of this paper is to present MR imaging of embedded fiducial markers as a method for tracking internal deformation of self-oscillating, scaled-up silicone VF models. MRI has been used to study laryngeal and vocal tract dynamics (e.g., Schlamann *et al.*, 2009; Echternach *et al.*, 2010; Zourmand *et al.*, 2014; Echternach *et al.*, 2015) and, along with ultrasound, is an attractive imaging modality due to absence of radiation risk for human subjects (as opposed to computed tomography, CT, imaging). In the study presented here, deformation in the VF phantoms was tracked via use of fiducial markers that, in MR images, exhibited contrast with the surrounding material. Since selection of marker material and type is application-specific, imaging studies were first conducted on static silicone phantoms in which the visibility of different candidate marker materials was explored. Two scaled-up, self-oscillating VF models were then fabricated, each containing one of the two marker types that showed most promise from the static studies. The vibrating models were scanned using a gated MRI gradient-recalled echo (GRE) sequence in which images of the models during different vibratory phases were reconstructed. The markers were readily identifiable in the MR images, allowing for tracking of internal deformation during vibration. In this paper, model fabrication methods, marker types, MRI protocol, and MRI test results are described and presented, and observations regarding limitations and future work are discussed.

II. METHODS

In this section the experimental methods and procedures are described. For additional information and details, the reader is referred to Taylor (2018).

A. Synthetic vocal fold model

The VF model was a homogeneous (one-layer), scaled-up, self-oscillating replica with exterior geometry similar to that of the “EPI” model of Murray and Thomson (2012). The model was fabricated using silicone Ecoflex 00-30 mixed with Silicone Thinner (Smooth-On, Inc.) at a 1:1:4 mixing ratio by weight (part A:part B:Thinner), which resulted in an elastic tangent modulus of around 2 kPa at approximately 20% strain (see Taylor, 2018, for stress-strain data). As discussed below, the model included embedded markers for tracking internal deformation during vibration.

Present limitations of MRI with respect to scan speed, resolution, susceptibility to motion artifacts, and signal-to-noise ratio (SNR) preclude the scanning of life-size models

that vibrate at frequencies typical of human phonation. In particular, the MRI protocol necessary to image periodic VF motion on the order of 100 Hz with adequate resolution for tracking of markers results in low SNR and unacceptable motion artifacts. For this study, these limitations were addressed by geometrically scaling up the VF model to simultaneously reduce both vibration frequency and spatial resolution requirements, thereby enabling the development of experimental protocols for MR imaging of these vibrating VF models.

The present study introduces the use of scaled-up self-oscillating VF models. Geometrically scaled-up VF models with prescribed (non-self-oscillating) motion have been used in voice research to reduce vibratory frequency to enable flow patterns to be studied using particle image velocimetry (PIV) (e.g., Erath and Plesniak, 2006; Krane *et al.*, 2007; Erath and Plesniak, 2010). Models in these studies achieved dynamic similarity with human phonation by matching Reynolds (Re) and Strouhal (St) numbers. Sidlof *et al.* (2011) used a model, scaled-up to 4× life size, comprised of silicone and springs to study flow separation data. One VF was fixed and the opposing VF underwent flow-induced vibrations. The springs primarily contributed to the degrees of freedom necessary for VF vibration, and the silicone was included to model collision between both the fixed and vibrating VFs. The stiffness of the spring was chosen to yield the desired frequency (10–14 Hz). In the present study, the model was scaled up to 4× life size, but entirely fabricated of silicone in order to simulate the motion of life-sized continuum-type self-oscillating VF models.

Simulations and experiments were first conducted to determine how scaled-up self-oscillating silicone VF models would respond compared to life-sized VF models. Three-dimensional finite element representations of the VF model, with geometric scales relative to human-sized models ranging from 1× (life-sized) through 5×, were created using the commercial code ADINA (ADINA R&D, Inc.) (see Fig. 1). A linearly elastic isotropic material model was used with an elastic modulus of 5 kPa, a density of 1000 kg/m³, and a Poisson’s ratio of 0.4. These properties were intended to be representative, although not perfectly matching, those of the silicone materials that would subsequently be used to fabricate the scaled-up models described below. Each model consisted of a mesh with element sizes of approximately 1/300 of the scale number, with 1260 nodes and 763 elements (i.e., the element size of the 4× model was 0.0133 m, or 1/300 of the scale number). Modal analysis was conducted on the models to quantify the relationship between *in vacuo* fundamental frequency (F₀) and model scale. The results in Fig. 2 show that F₀ was inversely proportional to the model scale, with a proportionality constant of 42.9. Consequently, the largest frequency drop occurred when the model was scaled from 1× to 2×, whereas the frequency drop was minimal from 4× to 5×.

The modal analysis results were compared with experimental results using self-oscillating scaled physical models and the setup shown in Fig. 3. As shown by Zhang *et al.* (2006), one-layer (homogeneous) self-oscillating VF models are acoustically coupled; i.e., they lock into frequencies close

FIG. 1. Finite element model for scaled-up VF model modal analysis, shown at one phase of the first predicted mode. Anterior, posterior, and lateral surfaces were fixed; other surfaces were free.

to the upstream tube resonant frequencies. As the intent of the present study was to generate flow-induced vibrations at the desired frequency, but not to necessarily precisely mimic human VF vibration kinematics (e.g., mucosal wave-like motion), an acoustically coupled model was deemed suitable. Subglottal tubing length for the experiments was selected based on the F0 predicted by modal analysis and the subglottal tube quarter-wavelength approximation

$$f = c/(4L), \quad (1)$$

where f is the frequency of the standing wave (intended to match F0), c is the speed of sound in air, and L is the tube length. A plenum was located between the air supply (Amatek DR083DC9Y, speed-controlled by a Powerstat 3PN136B variable transformer) and the subglottal tube to create an acoustic boundary. The length of the tubing

FIG. 2. Finite element model modal analysis results showing F0 vs model scale. Symbols denote finite element results. The dashed line is the curve fit corresponding to the inset equation.

FIG. 3. Experimental setup for measuring flow-induced vibratory properties of scaled models (not to scale).

downstream of the plenum was based on the model F0 found for each scaled model from modal analysis and the diameter was 2.45 cm. A funnel was designed for each model such that the same tubing diameter could be used for each model. The small diameter of the funnel matched the diameter of the tubing (2.45 cm diameter) and the large diameter of the funnel varied depending on the size of the model. The funnel was 7.25 cm in length. Onset pressure was measured using a pressure sensor (Omega PX26-005DV) located 2 cm upstream of the model. Frequency was measured using an electronic stroboscope (GenRad 1546 Strobosc® digital stroboscope). The parameters and results of the self-oscillating model tests are listed in Table I, in which it can be seen that the flow-induced vibration frequencies of the physical models followed the same general pattern predicted by the finite element models. Based on the finite element and experimental results, the 4× model was deemed to yield a sufficiently low frequency for MRI acquisition and was thus selected as the model to be used in the MRI experiments described below.

The Reynolds (Re) and Strouhal (St) numbers, defined below, were calculated to assess dynamic similarity of the 4× model with a previous 1× model and the human VFs:

$$Re = UD/\nu, \quad (2)$$

$$St = fD/U, \quad (3)$$

where $\nu = 1.5 \times 10^{-5} \text{ m}^2/\text{s}$ is the approximate kinematic viscosity of air, D is the maximum glottal opening, and U is a characteristic glottal jet velocity. Maximum glottal opening and estimated maximum glottal jet velocity for the 4× model

TABLE I. Tube lengths, onset pressures, and self-oscillation frequencies of 2×, 3×, and 4× scaled models.

Model scale	Tube length (m)	Onset pressure (kPa)	Frequency range (Hz)
2×	3.94	1.00	30–34
3×	5.90	0.30	20–22
4×	7.88	0.15	13–15

TABLE II. Reynolds and Strouhal numbers and corresponding variables for $1\times$ and $4\times$ models and human VFs. Note that the $4\times$ model glottal jet velocity represents a maximum over the glottal cycle, whereas the $1\times$ and human VF glottal jet velocities represent averages over the glottal cycle. Velocities vary with model characteristics such as stiffness and onset pressure. Consequently, the Re and St values here are approximations suitable for initial, order-of-magnitude comparison.

Model scale	Maximum glottal opening, D (m)	Glottal jet velocity, U (m/s)	Frequency, f (Hz)	Kinematic viscosity, ν (m^2/s)	Reynolds number, $\text{Re} = UD/\nu$	Strouhal number, $\text{St} = fD/U$
$1\times^{\text{a}}$	0.0027–0.0046	57–64	126–128	1.5×10^{-5}	10260–19630	0.0053–0.010
$4\times$	0.007	17.4	15	1.5×10^{-5}	8120	0.006
Human VF ^b	0.001–0.003	40	100–200	1.5×10^{-5}	2670–8000	0.0025–0.015

^aThomson (2004).

^bTriep *et al.* (2005).

were found experimentally, and values for maximum glottal opening and average glottal jet velocity from $1\times$ models and human VF studies were obtained from the literature (Thomson, 2004; Triep *et al.*, 2005). In the experiments, high-speed video (Phantom v1610, Vision Research Inc., 16 653 fps, 49 μs shutter speed) of the model vibration was used to determine the maximum glottal opening, D . Maximum glottal velocity, U , was estimated by injecting talcum powder into the flow upstream of the vibrating model and using high-speed video (same camera settings as for measuring D) to track powder particles exiting the glottis. The images were analyzed to obtain vector fields using DaVis 7.1 (Lavisision, Inc.) The results, listed in Table II, show that the Re and St of the current $4\times$ model compared reasonably well with $1\times$ model and human vocal fold data in the literature.

Because the $4\times$ self-oscillating model would be vibrating over an extended period of time during MRI scanning, tests were performed to assess consistency of model output vs time. The model was allowed to continuously vibrate for a period of 40 min, during which time frequency, subglottal pressure, and glottal area data were recorded every 5 min (see Taylor, 2018). Each parameter remained within 3% of its average value over the 40-min period, thereby demonstrating satisfactorily consistent model vibration.

B. Embedded markers for motion tracking

To determine which types of markers should be embedded into the $4\times$ model to track internal deformation, preliminary tests using static samples were conducted to identify markers that would be visible in the MR images. Candidates included markers that have been used for contrast in MR imaging (e.g., Schindel *et al.*, 2013; Xiao *et al.*, 2016) and those that do not create a signal in MR images (thereby providing contrast with silicone, which does create a signal). Different materials and patterns were tested, including variations in marker size and spacing to explore and optimize contrast and marker density. The materials tested include (see Taylor, 2018, for additional details, including manufacturer/supplier source and other material information): natural flake graphite powder with an average particle size of 5 μm , cupric sulfate 5-hydrate fine crystal, 529 mg/mL MultiHance gadobenate dimeglumine injection, titanium dioxide powder, 1 and 3 mm glass microbeads, agar made with a ratio of 5 g agar per liter of water, and synthetic black iron oxide powder. The graphite was tested in powder form as well as in

mixture form with 1:1:4 Ecoflex 00-30 at a weight ratio of 20 g Ecoflex to 3 g graphite powder. The cupric sulfate was sifted using a 0.15 mm sieve, and the powders consisting of particles less than 0.15 mm and particles greater than 0.15 mm were separately tested. The liquid MultiHance was evaporated and the resulting solid was ground into a powder. Similar to the cupric sulfate, the MultiHance powders were sifted using the 0.15 mm sieve and both particle sizes were tested.

The materials were tested by arranging markers in different layers of cylindrical 1:1:4 Ecoflex 00–30 silicone phantoms. The cylindrical mold in which the silicone was cast was 85 mm in diameter, which is the approximate size of the coronal face of two $4\times$ VF models in a full larynx configuration. Images of the static phantoms were acquired using a Siemens TIM-Trio 3 T MRI scanner at the BYU MRI Research Facility using a GRE pulse sequence and two dimensional (2D) magnetic resonance (MR) acquisition. The repetition time (TR) was 75 ms, the echo time (TE) was 2.18 ms, and the bandwidth per pixel was 558 Hz/Px. The slice thicknesses ranged from 3 to 5 mm. The images had a 160×160 mm field of view and a 128×128 matrix size, resulting in 1.25×1.25 mm spatial resolution. MR images of the selected markers in the static phantoms are shown in Fig. 4.

The results of the preliminary marker type tests are discussed further in Sec. III A, but in summary, the two types that were identified as most promising were the 3 mm glass beads and the cupric sulfate with particle size less than 0.15 mm. These two markers were subsequently each embedded in a VF model as follows; see Fig. 5 for illustration. Approximately half of the vocal fold model was fabricated by

FIG. 4. MRI images of static phantoms with selected markers. Top row, left to right: graphite, cupric sulfate (particles >0.15 mm), cupric sulfate (<0.15 mm), evaporated MultiHance (>0.15 mm), evaporated MultiHance (<0.15 mm). Second row, left to right: iron oxide, graphite mixed with silicone, glass beads (3 mm), glass beads (1 mm), agar. The two selected for further study in vibrating scaled-up VF models are outlined.

FIG. 5. (Color online) Renderings of $4\times$ VF models: (a) fabrication process; (b) mounting in custom shroud (coil—not shown—placed behind lip of the shroud); (c) MRI acquisition plane.

pouring 1:1:4 Ecoflex 00-30 into a VF-shaped mold and allowed to cure. Markers were applied to (or placed on) the silicone VF model surface and the remainder of the model was poured and allowed to cure. One of the VF models contained a grid of fine cupric sulfate powder (particles <0.15 mm) and the other model contained a grid of 3 mm glass beads. The resulting models contained one plane of a grid of markers somewhat near the anterior–posterior midplane (specifically, 28 mm from the posterior surface of the VF and 39 mm from

the anterior surface), a region that experienced large displacement during vibration. The two VF models were placed in a custom shroud where the posterior, anterior, and lateral sides were fixed to a wall (see Fig. 5). A custom radio frequency (RF) coil (15.24 cm, single loop, hydrogen) was placed on the lip of the shroud that surrounded the models.

C. MRI setup

The experimental setup used to scan the vibrating VF models is illustrated in Fig. 6. The pump and variable transformer described in Sec. II A supplied flow. The tubing upstream of the plenum was 7.92 m long and 2.54 cm in diameter. The flow source and plenum were located outside of the MRI room while the downstream tubing extended into the MRI room and connected to the model. The frequency of vibration was measured using the same subglottal pressure sensor as in Sec. II A. The sensor was located outside of the MRI room and connected to the subglottal tube (2 cm upstream of the model) via a 5 mm diameter flexible tube that extended into the MRI room. The sensor was connected to a data acquisition system (National Instruments cDAQ-9178 chassis with NI-9239 voltage input module) to record the frequency via LabVIEW. The pressure signal was amplified (AD620-based amplifier, DROK part number 200315) and fed into a waveform generator (DG1022, Rigol Technologies, Inc.) to create a TTL signal to trigger the MRI machine.

Three sets of images were obtained during model vibration. Set A consisted of 2D images (i.e., single slices), ensemble averaged ($N=10$), with the image plane coinciding with the plane of markers as shown in Fig. 5. Images at 11 phases, in addition to when the model was at rest, were acquired. Set B was the same as A, but with only a single image (no averaging) in order to determine the influence of averaging. Only images at rest and at a single phase during vibration were obtained for Set B. Set C consisted of 3D images (no averaging) of the entire model at two phases of oscillation. MRI and other parameters for these three cases are listed in Table III and are described further below.

FIG. 6. Experimental setup for MR imaging of VF models.

TABLE III. MRI sequence and other parameters for the three imaging sets.

	Set A	Set B	Set C
Pulse sequence	GRE	GRE	GRE
Acquisition type	2D	2D	3D
Matrix size	256 × 256	256 × 256	128 × 128 × 72
Field of view	128 × 128 mm	128 × 128 mm	128 × 128 × 72 mm
In-plane resolution	0.5 × 0.5 mm	0.5 × 0.5 mm	1 × 1 mm
Slice thickness	4 mm	4 mm	1 mm
Echo time (TE)	2.71 ms	2.75 ms	2.1 ms
Bandwidth	592 Hz/Px	528 Hz/Px	797 Hz/Px
Flip angle	10°	10°	10°
Number of averages	10	Single	Single
Total scan time for one image	2 min 53 s to 6 min 7 s	18 s to 37 s	10 min 40 s to 11 min 7 s
Model frequency during scan	14.7 Hz	14.7 Hz	14.8 Hz
Subglottal pressure during scan	0.19 kPa	0.19 kPa	0.18 kPa

The same scanner indicated in Sec. II B was used for all imaging studies. Signal intensity in the silicone model was optimized as described by Taylor (2018), resulting in the scan settings listed in Table III.

1. Set A: Single-slice scan, ten averages

A standard 2D or 3D Cartesian k-space trajectory was used for all MR acquisitions. The MRI sequence was triggered as described above at a given phase such that one line in k-space was acquired at each cycle. Once all lines had been acquired (i.e., one image) over ten averages, the built-in MRI delay was set to 6 ms for acquisition of an image at the next phase. This process was repeated, incrementally increasing delay by 6 ms, until all 11 phases were captured. The actual delay time likely deviated slightly (potentially as much as ± 2.5 ms) from the nominal setting due to temporal quantization of trigger acquisition time. A scan with the model at rest was also performed.

High-resolution 2D images were acquired using a 128×128 mm field of view and a 256×256 matrix size, resulting in 0.5×0.5 mm spatial resolution. The slice thickness was 4 mm. The TR was determined by the external trigger. Scan time was reduced to decrease blurring via 3/4 partial Fourier phase acquisition. Contrast and SNR were increased via averaging ($N=10$). The scan time with the model at rest with ten averages was 2 min 53 s. The scan time with the vibrating model with ten averages ranged from 3 min 50 s to 6 min 7 s for the different phases, depending on the MRI delay setting and small cycle-to-cycle fluctuations in triggering and periodicity. The total time to capture 11 phases was just over approximately 48 min. The model frequency and subglottal pressure during imaging were 14.7 Hz and 0.19 kPa, respectively.

2. Set B: Single-slice scan, no averaging

Set B was the same as Set A, but without averaging. Scans at one phase and with the model at rest were performed. The scan time with the model at rest was 18 s and the scan time with the model vibrating was 37 s. As noted above, the dynamic scan time would vary if multiple phases

were to be captured. Frequency and subglottal pressure during imaging were 14.7 Hz and 0.19 kPa, respectively.

3. Set C: 3D scan, no averaging

High-resolution 3D volumetric scans were acquired using a $128 \times 128 \times 72$ mm field of view and a $128 \times 128 \times 72$ matrix size resulting in $1 \times 1 \times 1$ mm resolution. Scan time was decreased through 3/4 phase partial Fourier acquisition. Scans at two phases were performed, with the 3D scan time at one phase being 10 min 40 s and 11 min 7 s at the other phase. Frequency and subglottal pressure during imaging were 14.8 Hz and 0.18 kPa, respectively.

III. RESULTS AND DISCUSSION

A. Marker selection

Images of the marker-testing phantom are shown in Fig. 4. The two materials that exhibited the best contrast with minimal distortion were the fine cupric sulfate crystals (particles <0.15 mm) and the 3 mm glass beads. Fine (<0.15 mm) and coarse (>0.15 mm) cupric sulfate crystals both yielded good contrast, but the coarse cupric sulfate generated large disturbances in the magnetic field. The fine cupric sulfate markers were nominally 1 mm in diameter and 0.4 mm thick. The markers were approximately 4 mm apart from edge to edge. The marker diameter in the MRI data, as measured using imaging software, ranged from 2 to 3.5 mm. The geometric inaccuracy, or the difference in size between the real markers and the markers as they appeared in the image, was due to disturbance in the magnetic field caused by the cupric sulfate–Ecoflex interface. The interface of two materials with different magnetic susceptibilities results in local distortion in the magnetic field which could contribute to the geometric inaccuracy (Elster, 1993). Geometric inaccuracy also resulted from the powder spreading during the pouring of the top layer in the fabrication process. In comparison with the glass beads, the cupric sulfate markers were powder-based, and thus less intrusive and more unlikely to alter the model vibration. The cupric sulfate also allowed for higher spatial resolution than the glass beads.

FIG. 7. Left: Pictures of markers in models before pouring second layer. Right: MRI image of static models. In both image sets, the cupric sulfate markers are at the top and the glass beads are at the bottom.

The 3 mm glass spheres were approximately 3.5 to 4 mm apart from edge to edge. The marker diameters as measured in the MRI images ranged from approximately 3.5 to 4 mm. The glass beads were readily visible, but because of increased mass, more likely to affect the movement of the VF models. The volume fraction of the glass beads to the entire model was 0.0038 (or 0.38%), and the volume fraction of the glass beads to the volume of a 3 mm-thick coronal layer of the model was 0.0939 (9.39%). The densities of Ecoflex 00-30 and the glass beads are approximately 1065 and 2518 kg/m³, respectively. The small volume fraction of glass beads (less than 0.1% of the whole model and less than 10% of the 3-mm-thick marker plane) lessened the degree to which the beads altered the model vibration despite the differences in density and stiffness. For example, modal analysis predicted that adding 3 mm glass beads would decrease the *in vacuo* fundamental frequency by less than 1%. However, use of multiple layers of beads may be inadvisable

due to a greater anticipated effect on model vibration. The glass beads were deemed acceptable for this study with only one layer of markers, but in future studies with multiple layers, further investigation into the effect of the beads on the vibratory pattern would be needed.

B. Vocal fold phantom results

MR images of VF models at rest (i.e., no flow) with markers are shown in Fig. 7, along with camera-acquired pictures of the markers during the fabrication process. Both markers were, in reality, circular, but appear with cross shapes in the MR images due to the magnetic field patterns resulting from the interfaces of materials with different magnetic susceptibilities.

Results of the Set A (single-slice, averaged) dynamic scan are shown in Fig. 8. The cupric sulfate and glass beads remain clearly visible in the dynamic images throughout vibration. The glass beads have more distinct outlines than the cupric sulfate, although both sets of markers are sufficiently clear for identification of their centroids. The profiles of the VF models are distinct throughout the cycle, although a small amount of blurring, most likely due to high velocity, is evident near the medial surfaces at some phases. The minimal blurring demonstrates that the acquisition time for one line in k-space was sufficiently short (1.7 ms) in comparison to the period (68 ms) and that triggering from the pressure signal was suitable for acquiring specific phases.

The cupric sulfate yielded better spatial resolution than the glass beads, in large part due to the smaller footprint of the cupric sulfate markers. The glass beads, on the other hand, are somewhat more clearly distinguishable and exhibit less blurring than the cupric sulfate in regions experiencing high velocity (i.e., near the medial surfaces while the model was opening and closing). The glass beads remained clearly visible during these phases of maximum velocity (e.g., around phases I-J) whereas some of the cupric sulfate

FIG. 8. Images from Set A spanning a full vibration cycle with different trigger delays between successive images. To reconstruct this representative glottal cycle, the phases have been reordered from their original acquisition order. See supplementary material¹ for an animation of the images.

markers were harder to resolve. Due to minimal blurring, the glass beads would thus be expected to be easier to track and exhibit less location-finding error.

Some cupric sulfate markers in the F and G phase images near the medial and medial-superior surfaces are somewhat blurred. At these phases, the model was near maximum opening and the velocity would have been less than at other phases. The blurring at these phases are possibly due to cycle-to-cycle variations in model motion during image acquisition. The distortion of the cupric sulfate in these regions appears to still be sufficiently small to enable centroids of nearly all markers to be reliably located and tracked throughout the cycle.

The general decrease in brightness from the lateral to the medial edges of the VF models is an artifact of the coil surrounding the VF model shroud. The lateral edges of the VF models are closest to the coil (Fig. 5), resulting in a stronger signal at the lateral vs medial regions of the VF models (Jones and Witte, 2000). This non-uniformity could present a slight challenge when determining appropriate pixel intensity thresholds for automated marker identification and tracking; however, it is anticipated that this could be overcome by image filtering during post-processing.

The influence of averaging can be seen by comparing the averaged (Set A) and non-averaged (Set B) scans in Fig. 9. As would be expected, SNR of the averaged images is better than non-averaged images for models both at rest and during vibration. There is minimal difference between the

FIG. 9. Averaged (left) and non-averaged (right) MRI images from Sets A and B, respectively. Top row: Images of the models at rest. Bottom row: Images of the models at one phase of vibration.

FIG. 10. (Color online) 3D segmentation of MR-imaged vibrating VF models at one phase from Set C scans. Top: frontal view. Bottom: Perspective view with transparency enabled for marker visibility (left: glass beads, right: cupric sulfate).

two still images in terms of marker visibility and VF profile clarity. Nearly all markers are identifiable in the non-averaged dynamic image, although there are a few cupric sulfate markers near the medial-surface margin that cannot be precisely located due to model motion artifacts. These markers can be more clearly distinguished in the averaged image. The VF profile is also generally clearer in the averaged image.

Segmentations from the 3D scan (Set C) are shown in Fig. 10. Over the approximately 11-min scan time, the model vibration was sufficiently stable for the final 3D image to be clear, with minimal blurring of edges and suitable marker visibility. This demonstrates the ability of the 3D scan to resolve the entire model profile and tracking markers during vibration. Even though the model vibration consistency is such that the long scan times required for additional phases would be feasible, it is anticipated that future advances in MRI hardware and sequencing will lead to shorter scan times, improving the outlook for application of 3D scans such as shown here.

IV. CONCLUSION

This study describes an MRI-based method for tracking the internal deformation field of scaled-up ($4\times$), self-oscillating VF models. The model was scaled up to yield a sufficiently low flow-induced vibration frequency to enable imaging using MRI technology. Tests showed that the $4\times$ model exhibited reasonable dynamic similarity with life-size models. Several materials were explored as potential tracking markers, with two—cupric sulfate and 3 mm glass beads—being identified as the most promising candidates. Both markers exhibited adequate contrast with the silicone VF model material to the extent that they could be readily identified in MR images. Potential applications include validation of internal stress and strain predicted by computational models, estimates of stress and strain in human-sized VF models based on dynamic similarity, acquisition of internal deformation fields to complement bioreactor studies, and

possible future additional experiments using scaled-up, self-oscillating models.

A gated MRI protocol for imaging the VF model during vibration was developed. The protocol used the conditioned subglottal pressure as a trigger source to capture specific phases. Both 2D (averaged as well as non-averaged) and 3D (non-averaged) image sets were acquired of the model at rest and at different phases during vibration. The images were shown to exhibit suitable contrast and SNR for marker tracking. Although smaller markers are preferable since they are potentially less intrusive and can yield improved spatial resolution, the smaller markers in the results shown here were more susceptible to blurring. Further study of this is required. Using an MRI machine that does not limit parameter settings based on human subject safety and has a stronger magnetic field could lead to clearer images with smaller markers.

The present study is intended to be a step towards internal imaging of life-sized VFs and VF models, and as such, several observations are worth noting. One of the primary limitations of this study is the need for a scaled-up model to lower the vibration frequency. Further developments, including the use of MRI facilities with increased magnetic field strength, development of different acquisition protocol, and optimized RF coils, may yield improvements in temporal resolution and signal-to-noise ratio that will allow for studies such as this to be performed using life-sized synthetic models as well as excised larynges. In addition, even though MRI is capable of distinguishing between tissue types, it is anticipated that markers would need to be used in excised larynges for more precise displacement tracking. The 3 mm glass beads used in the present study would be too large for life-sized synthetic models and excised larynges; consequently, further study of marker types and placement will be needed. Regarding life-size synthetic models, alternative ways of placing markers will also likely need to be explored, particularly for models with complex features such as embedded fibers and multiple layers. In such cases, microinjection of slurries containing contrast materials such as those discussed herein may be a viable approach for marker placement.

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¹See supplementary material at <https://doi.org/10.1121/1.5091009> for animation of model vibration reconstructed using the images in Fig. 8.

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