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Piehler et al: Motion-Corrected Late Gadolinium Enhancement

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Abstract

***Background*—**Routine clinical use of novel *free-breathing, motion-corrected, averaged* late gadolinium enhancement (moco-LGE) cardiovascular magnetic resonance may have advantages over conventional breath held LGE (bh-LGE) especially in vulnerable patients.

***Methods and Results*—**In 390 consecutive patients, we collected bh-LGE and moco-LGE with identical image matrix parameters. In 41 patients, bh-LGE was abandoned due to image quality issues, including 10 with myocardial infarction (MI). When both were acquired, MI detection was similar (McNemar test, $p=0.4$) with high agreement (kappa statistic 0.95). With artifact-free bh-LGE images, pixelwise MI measures correlated highly ($R^2=0.96$) without bias. Moco-LGE was faster, and image quality and diagnostic confidence were higher on blinded review ($p<0.001$ for all). Over a median of 1.2 years, 20 heart failure hospitalizations and 18 deaths occurred. For bh-LGE, but not moco-LGE, inferior image quality and bh-LGE non acquisition were linked to patient vulnerability confirmed by adverse outcomes (logrank $p<0.001$). Moco-LGE significantly stratified risk on the full cohort (logrank $p<0.001$), but bh-LGE did not (logrank $p=0.056$) since a significant number of vulnerable patients did not receive bh-LGE (due to arrhythmia or inability to breath hold).

***Conclusions*—**MI detection and quantification are similar between moco-LGE and bh-LGE when bh-LGE can be acquired well, but bh-LGE quality deteriorates with patient vulnerability. Acquisition time, image quality, diagnostic confidence and the number of successfully scanned patients are superior with moco-LGE which extends LGE-based risk stratification to include patients with vulnerability confirmed by outcomes. Moco-LGE may be suitable for routine clinical use.

Key Words: myocardial delayed enhancement, magnetic resonance imaging, myocardial infarction

Novel *free-breathing, motion-corrected, averaged* cardiovascular magnetic resonance (CMR) with late gadolinium enhancement (LGE)[1] for the detection and quantification of myocardial infarction (MI) and scar introduces several important advantages for routine clinical use. This technique is a key component of an emerging "free-breathing CMR" paradigm[1-5] that liberates patients and clinicians from significant constraints. Conceptually, without a mandate for breath holding or even sinus rhythm, free-breathing CMR scanning may be: 1) less taxing to the patient and technologist who otherwise must coordinate their efforts; 2) more efficient, given the absence of delays between breath holds or repeated acquisitions which are pronounced with frail patients; 3) more robust diagnostically, yielding high image quality with higher signal to noise ratios (averaging) and freedom from ghosting artifacts (common in breath held acquisitions);[1] and 4) more consistent and generalizable, extending these capabilities to more vulnerable patients with dyspnea, arrhythmia, and other comorbidity who can be challenging to image. Imaging vulnerable patients is especially important since MI is more prevalent in such patients: those who are older, those with heart failure and those with atrial fibrillation—groups who may be unable to breath hold adequately. Thus, the "free-breathing CMR" paradigm for LGE may represent an important advance in CMR worthy of further study.

CMR must provide robust LGE capability for all patients referred for CMR since subclinical disease is common. Indeed, the burden of MI in the general population is considerably higher than previously appreciated given the high prevalence of clinically unrecognized MI detected by LGE that is prognostically adverse.[6-9] LGE for detecting MI has been validated and predicts adverse events in large populations.[6, 10-18] Yet, prior studies suggested limitations associated with free-breathing single shot "subsecond" LGE compared to conventional segmented breath held LGE,[19-21] highlighting a need for further improvement in free-breathing techniques to detect MI.[22] Subsequent innovation has introduced fully automated in-plane motion correction (with nonrigid deformation) to co-register a series of higher spatial resolution "single shot" images followed by averaging to increase signal to noise ratios.[1, 22] This methodology yields consistently high quality LGE images.[1, 22]

To investigate the clinical performance of respiratory motion-corrected, free-breathing averaged LGE (moco-LGE), we compared it against conventional breath held segmented LGE (bh-LGE) acquired contemporaneously for a consecutive series of patients referred for CMR. We hypothesized that: 1) blinded image quality and diagnostic confidence assessments would be superior for moco-LGE; 2) acquisition times would be shorter for moco-LGE; 3) pixelwise quantitative assessments of MI size would correlate highly without bias compared to high quality bh-LGE images that were free of artifacts; 4) with blinded interpretation in a series of consecutive patients undergoing CMR, moco-LGE would detect a similar proportion of MI in the cohort as bh-LGE; and 5) moco-LGE would predict adverse events similarly to bh-LGE. Collectively, these efficacy data (infarct size comparisons) and effectiveness data (image quality/confidence ratings and outcomes predictions in a real life clinical practice setting) may advance our acceptance and understanding of moco-LGE as well as the merits of the free-breathing CMR paradigm.

Methods

Patient Population

After Institutional Review Board approval, we prospectively recruited 390 adult patients referred for clinical CMR with contrast at the UPMC CMR Center at the time of their CMR scan from April 18th to November 18th 2011 and followed them through November 10th, 2012. This cohort was formed *a priori* to examine whether novel LGE techniques were diagnostically robust and predicted patient outcomes. Inclusion criteria were written informed consent and completion of a contrast enhanced CMR scan which required a glomerular filtration rate ≥30 mL/min/1.7m^2, and no other contraindications to CMR. Comorbidity data were determined according to the medical record acquired at the time of CMR scanning and informed consent. Study data were managed using REDCap (Research Electronic Data Capture) electronic data capture tools hosted at the University of Pittsburgh.[23] Vital status was ascertained by Social Security Death Index queries and medical record review. Hospitalizations for heart failure were identified by electronic chart review of UPMC records. There were no exclusion criteria. Our clinical practice is to accept referrals regardless of frailty.

CMR Scans

All patients received clinical CMR scans by 2 dedicated CMR technologists with a 1.5 Tesla Siemens Magnetom Espree (Siemens Medical Solutions, Erlangen, Germany) and a 32 channel phased array cardiovascular coil. The exam included standard breath held segmented cine imaging with steady state free precession (SSFP) in short axis (6 mm slice thickness with 4 mm gap) and 2-, 3-, and 4-chamber orientations (image matrix 256 x ~144, acceleration factor (GRAPPA) 3). When patients could not breath hold or had significant arrhythmia, we employed real time cine imaging (image matrix 256 x ~96, acceleration factor (GRAPPA) 4)

Conventional Late Gadolinium Enhancement. Breath held late gadolinium enhancement (bh-LGE) imaging with segmented fast low-angle shot gradient echo readouts was performed 10 minutes after a 0.2 mmol/kg intravenous gadoteridol bolus (Prohance, Bracco Diagnostics, Princeton, NJ). To optimize LGE, we used a phase sensitive inversion recovery (PSIR) pulse sequence to increase signal to noise ratios, correct for surface coil intensity variation, and render signal intensity proportional to T1 recovery.[24] This sequence acquires inversion recovery and proton density weighted data every other heart beat (with every third heart beat for faster heart rates>100 bpm). PSIR yields constant infarct size over a variety of inversion times,[24] and LGE yields constant infarct size measures between 10 and 30 minutes after contrast.[25] Typical parameters included an adiabatic 180 degree inversion pulse every 2nd R-R, FOV 38 x 32 cm, matrix 256 x 144 (typical phase matrix range 128-160) with lower phase matrix for faster heart rates (e.g., 128), 6 mm slice thickness with 4 mm gap for short axis stacks, TR/TE 8.3 msec/3.2 msec, FLASH flip angle 25 degrees, 20 views per segment, inversion time ~300 msec (adjusted for nulling noninfarcted myocardium), pixel bandwidth 140 Hz, and acceleration factor (GRAPPA) 2. Typical breath holds were 10 heartbeats in duration, including discarded beats to ensure steady state.

Free-Breathing Motion-Corrected Late Gadolinium Enhancement. After acquisition of bh-LGE images, respiratory motion-corrected, free-breathing single shot steady state free precession (SSFP), averaged PSIR images (moco-LGE)[1] were acquired with identical spatial resolution, FOV, slice thickness, and slice location as the conventional breath held segmented FLASH LGE images with optimized inversion time for nulling. Typical SSFP readout parameters were TE 1.65 msec, pixel bandwidth 977 Hz, acceleration factor (GRAPPA) 2, and flip angle 50 degrees. Each acquisition had 8 repeated measurements per slice with each measurement every 2nd R-R interval (every 3rd for faster heart rates>100 bpm) over a duration of 16 heart beats (or 24 heart beats for faster heart rates>100 bpm). Fully automated in-plane respiratory motion compensation was achieved performing independent nonrigid registration processes to a reference frame with respect to all the other frames in the complete set of acquired images. Each independent registration step implemented an optimization procedure that minimizes a similarity measure of the two images to find the best transformation that maps a given frame into the frame of reference described previously,[1] a process representing an "image-based navigator" scheme.

The averaged image resulting from averaging of the *most similar* 4 of the 8 (i.e., 50%) single shot images provided the most reliable image quality since inclusion of all 8 single shot images (100%) might introduce uncompensated through plane motion. The moco-LGE technique corrects in-plane motion only and cannot correct for through-plane motion. Averaging 4 images doubles signal to noise (SNR) where SNR improvement= square root(# averages).[1]

Image Analysis

We compared separate blinded image analysis comparing moco-LGE and bh-LGE on the basis of: 1) pixelwise infarct size measures, 2) acquisition time, 3) image quality scores, 4) image confidence scores, and 5) ability to stratify risk of subsequent outcomes in the full cohort of consecutive patients. We had no histologic gold standard in this clinical cohort and did not use the clinical report for analysis which may have been influenced by either bh-LGE or moco-LGE. Acquisition times for short axis LGE stacks were obtained from the time stamps on the first and last image of the stack. MI was identified when LGE involved the subendocardium in a coronary distribution; other “atypical” patterns of LGE were specifically not designated as MI. This strategy yields sensitivities and specificities >90% for MI detection.[6, 13, 26-28] Among 41 individuals with high image quality on bh-LGE images that were otherwise chosen arbitrarily, we quantified infarct size from short axis stacks of LGE images where there is minimal through plane motion.[1] Computer-assisted planimetry using Medis QMass software (version 7.2, Leiden, The Netherlands) quantified MI mass (blinded) using the full width at half maximum (FWHM) technique, an accepted technique for LGE quantification.[29]

We employed subjective image quality ratings blinded to clinical interpretation and outcomes. Similar to Sievers et al.,[20] we rated image quality (1=very poor and not analyzable, 2=poor, 3=acceptable, 4=good, 5=very good) and rated the degree of observer confidence with regard to the presence or absence of infarction (1=low confidence, 2=some confidence, 3=high confidence). Images were interpreted by 3 experienced observers blinded to clinical status and to the observers' interpretation of the corresponding moco-LGE or bh-LGE image, performed on different day. The bh-LGE and moco-LGE images each have their own identifiable characteristics since the artifact type (chest wall ghosting), noise levels, and contrast between different chemical species (blood, myocardium, fat, etc) makes it easy to distinguish the LGE pulse sequence to the experienced observer. Therefore, we made no attempt to blind observers to the LGE technique.

Statistical Analysis

Categorical variables were summarized as percentages, and continuous variables were summarized as median with first and third quartiles (Q1-Q3), since continuous variables exhibited skewed distributions on visual inspection, and the Shapiro Wilk test indicated non normal distributions. Statistical tests were two sided, and $p<0.05$ was considered significant. The Wilcoxon signed rank sum test compared acquisition time data between pairs of bh-LGE and moco-LGE images. Chi square tests or Fisher exact tests compared categorical variables. Bowker's test of asymmetry assessed agreement between image quality and image confidence rating for bh-LGE and moco-LGE. McNemar's statistic tested whether there were any significant differences in the diagnosis of MI by moco-LGE or bh-LGE, and Cohen's kappa statistic assessed agreement for MI detection between moco-LGE and bh-LGE. Wilcoxon rank sum tests compared continuous variables. Linear regression, correlation plots, and Bland-Altman compared infarct size measures. Logistic regression modeled odds of poor image quality. To compare risk stratification between moco-LGE and bh-LGE, survival analysis for all cause mortality and heart failure hospitalization employed the logrank test and Cox regression. Statistical analyses were performed using SAS 9.2 (Cary, NC) and Microsoft Excel (Redmond, Washington).

Results

Patient Characteristics

The characteristics of the sample are summarized in Table 1 according to whether or not myocardial infarction was recorded in the clinical report. Overall, 20% (77/390) of the sample exhibited MI on LGE images according to the clinical report. Both bh-LGE and moco-LGE images were available to the physician responsible for the scan. No adverse events occurred.

Free-Breathing, Motion-Corrected, Averaged LGE versus Breath Held Segmented LGE

Examples of good LGE image quality for bh-LGE and moco-LGE acquisitions are shown in Figure 1; examples of artifacts encountered with bh-LGE are shown in Figure 2 with accompanying moco-LGE images. While all patients received moco-LGE, there were 41 patients in whom bh-LGE was abandoned due to poor image quality (e.g., on preceding breath held cine attempts) or patient's inability to breath hold where only free-breathing single shot and moco-LGE were acquired. Real time cines were used for functional assessment when patients had arrhythmia or could not breath hold earlier in the course of CMR exam; 25 of the 41 individuals (61%) without bh-LGE images used real time cines, whereas only 25 of 349 patients (7%) with bh-LGE images employed real time cines. Significantly fewer patients received bh-LGE (i.e., 89% (95% CI 85% - 92%)) compared to moco-LGE (100%, (p<0.001), including 10 with MI. An example of a case where bh-LGE was not performed is shown in Figure 3 where moco-LGE data yielded exactly opposite results compared to noninvasive testing culminating in excellent patient outcome with near complete recovery of left ventricular function that was profoundly dysfunctional at baseline. A history of atrial fibrillation was associated with higher odds of fair image quality by moco-LGE (OR 8.6 95%CI 2.45-30.0) and non acquisition of bh-LGE (OR 5.81 95%CI 1.99-16.9).

We examined acquisition times in a subset of 100 consecutive patients from September 26, 2011 to November 18, 2011, that had bh-LGE acquired. Free-breathing, moco-LGE was significantly faster than bh-LGE (median 160 sec (Q1-Q3 139-182 sec) versus 331 sec (Q1-Q3 291-359 sec); p<0.001) as shown in Figure 4. Free-breathing, moco-LGE yielded higher image quality than bh-LGE based upon the rating schemes when both types of images were acquired (Table 2). Similarly, moco-LGE provided higher diagnostic confidence (Supplementary Table) than bh-LGE based upon the rating schemes. These findings were consistent across all three observers.

There was excellent agreement between moco-LGE and bh-LGE for detecting MI with only 6 cases (1.7%) among 347 pairs of moco-LGE and bh-LGE images yielding disagreement on blinded review. In 4 individuals, MI was noted only on bh-LGE, and in 2 individuals, MI was noted only on moco-LGE. The extent of disagreement was not significant (McNemar's test, p=0.41). Cohen's kappa statistic was 0.95 (95% CI 0.90-0.99) revealing high agreement.

Quantitative MI size measurements on a subset of 41 patients with excellent bh-LGE image quality showed nearly identical values compare to quantitative MI size measurements from moco-LGE images across the MI size spectrum (Figure 5). The correlation was high with the regression line approximating the unity line with a slope of nearly 1.0 and a y-intercept of nearly zero. Bland-Altman plots revealed excellent agreement across the MI size spectrum (Figure 5).

Survival analysis

Over a median follow-up of 1.2 years (Q1-Q3 1.1-1.4 yrs), there were 36 total events: 18 hospitalization for heart failure of whom 2 died and 16 additional deaths. Lower image quality and non acquisition for bh-LGE was related to increased patient vulnerability as confirmed by their outcomes (logrank $p<0.001$) as shown in Figure 6; those who did not receive bh-LGE were a particularly vulnerable group (10 events among the 41). There remained a significant association between vulnerability determines by adverse outcomes and lower *image quality* for bh-LGE when: 1) we conservatively recoded missing bh-LGE data as "3 = acceptable" (HR 2.90, 95%CI 1.57-5.34 for every decrement in image quality); or 2) we ignored the 41 patients without bh-LGE (HR 2.18, 95%CI 1.01-4.71 for every decrement). Similar trends were observed for *observer confidence* when missing data for bh-LGE were ignored (HR 2.58, 95%CI 0.97-6.84 for every decrement) or recoded as 1 = low confidence (HR 2.03, 95% CI 1.41-2.93 for every decrement), or 2 = some confidence (HR 3.38, 95%CI 1.74-6.57 for every decrement).

There were no such relationships for moco-LGE (Fig. 6); moco-LGE *image quality* was *not* related to outcomes (HR 1.08, 95%CI 0.52-2.26 for every decrement), and there was no association between moco-LGE *observer confidence* and outcomes (HR 0.47, 95% CI 0.06-3.40

for every decrement). The moco-LGE technique was able to stratify risk significantly on the full cohort (logrank p=0.01), but the bh-LGE technique was not (logrank p=0.056) since a significant number of vulnerable individuals did not receive bh-LGE (Figure 6). Survival analysis results did not change significantly when excluding 64 (16%) survivors who may not have followed up at our institution

Discussion

This study used moco-LGE to investigate the free-breathing paradigm for LGE in a consecutive cohort of 390 patients referred for clinical CMR. The principal findings of our study were that free-breathing, motion-corrected, averaged LGE (moco-LGE) outperformed conventional breath held segmented LGE (bh-LGE) in terms of acquisition time, image quality, diagnostic confidence, and the number of patients in whom high quality LGE could be acquired with clinician confidence. These characteristics extend LGE-based risk stratification to include patients with vulnerability confirmed by increased mortality and incident heart failure hospitalization. These vulnerable patients were challenging to image successfully with bh-LGE. Indeed, patients in whom bh-LGE was abandoned or suboptimal were the patients most prone to adverse outcomes. The moco-LGE technique yielded similar quantitative MI size measures compared to artifact-free bh-LGE across the MI size spectrum without evidence of bias. Also, moco-LGE and bh-LGE did not exhibit significant differences in the diagnosis of MI when bh-LGE could be acquired. These efficacy data (infarct size comparisons) and effectiveness data (relationship between image quality/confidence ratings and outcomes in a clinical practice setting) suggest moco-LGE is robust.

Our study illustrates a fundamental limitation of breath holding techniques: they fail to bring the advantages of CMR to all referred patients. Image quality and diagnostic confidence for bh-LGE were associated with outcomes, whereby those with worse images were the most vulnerable as demonstrated by their event rates. These data suggest that breath holding techniques struggle in the most vulnerable patients where the need for robust characterization is the highest. This observation did not apply to moco-LGE which highlights a critical advantage of the free-breathing paradigm: patient vulnerability does not appear to compromise image quality. Therefore, we highlight a potential need for vendors to develop free-breathing techniques for all CMR pulse sequences to bring the advantages of CMR to all patients.

Given the inherent importance of detecting MI with LGE,[6-11] including the large burden of unrecognized MI in the community,[6] these data have important implications for CMR practice. Based on our results and our clinical experience, we believe moco-LGE is ready for routine clinical use, perhaps as the primary LGE technique. Further study of the clinical performance of moco-LGE would be useful to confirm its clinical utility.

Our data differ from the findings of Sievers et al[21] who reported inferior performance when free-breathing techniques were used with a single measurement at lower spatial resolution (e.g., 104x192). The main difference in our methodology was: 1) enforcement of higher spatial resolution for moco-LGE, identical to bh-LGE, and 2) the application of novel motion correction and averaging techniques to increase signal to noise ratios from averaging of automatically coregistered images that employed "image-based navigators." The improvement in signal to noise ratios with moco-LGE and the lack of ghosting artifacts are clinically important advantages that we believe significantly improve reader confidence. The beneficial effects of *averaging motion-corrected* images are an important technical advance in CMR that may not yet be widely appreciated by the CMR community. The ranking of image similarity measures is also an important advantage to minimize effects of through plane motion, especially in long axis image orientations, since through plane motion will diminish image similarity. To minimize the breath hold, our bh-LGE protocol used parallel imaging. Omitting parallel imaging would only prolong the breath hold, worsen motion artifacts, and strengthen the case for moco-LGE.

Limitations

Our study has limitations. First, our data are from a single center referral population so results may not generalize. We enrolled consecutive patients to minimize this limitation. Second, the order of bh-LGE and moco-LGE was not randomized, so delayed washout may have favored moco-LGE with enhanced blood pool-MI contrast. We believe the differences are minor, especially since LGE is reproducible between 10 and 30 minutes with minimal changes in the partition coefficient. Third, some bh-LGE imaging attempts were abandoned by the clinician in charge of the clinical study (breaching the study protocol) so comparison of image quality (efficacy) could not be performed for these patients. Still, our data from a purely clinical population may better reflect expected clinical practice (effectiveness). Poor outcomes in those where bh-LGE was abandoned suggest underlying frailty and less ability to execute breath holding successfully. Fourth, the futility of blinding of the bh-LGE and moco-LGE techniques made it impossible to exclude bias corrupting image quality ratings that were blinded to all other clinical data. We used multiple observers and examined multiple aspects of LGE performance including pixelwise MI size assessments to minimize this bias.

Conclusions

The efficacy data (infarct size comparisons) and effectiveness data (relationship between image quality/confidence ratings and outcomes in a clinical practice setting) suggest moco-LGE is robust. The advantages provided by moco-LGE extend LGE-based risk stratification to include vulnerable patients who may be challenging to image successfully with conventional bh-LGE. The moco-LGE technique may be suitable for routine clinical use.

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Disclosures

None.

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Table 1. Patient characteristics (n=390)

Variable	Myocardial infarction N=77 Frequency (n) or Median (Q1-Q3)	No Myocardial infarction N=313 Frequency (n) or Median (Q1-Q3)	P value
Demographics			
Age (years)	64 (55-72)	54 (40-64)	<0.001
Female	29% (n=22)	47% (n=146)	0.004
White race	87% (n=67)	84% (n=263)	0.52
Black race	8% (n=6)	13% (n=40)	0.32
General Indication for CMR exam			
Known or suspected cardiomyopathy	26% (n=20)	44% (n=137)	0.004

Possible coronary disease/viability/vasodilator stress testing	77% (n=59)	36% (n=112)	<0.001
Vasodilator stress testing	48% (n=36)	23% (n=74)	<0.001
Evaluation for arrhythmia substrate	5% (n=4)	31% (n=97)	<0.001
Adult congenital heart disease	1% (n=1)	3% (n=10)	0.24
Mass or thrombus	9% (n=7)	3% (n=10)	0.025
Comorbidity			
Diabetes	34% (n=26)	13% (n=42)	<0.001
Hypertension	74% (n=57)	39% (n=123)	<0.001
Dyslipidemia	62% (n=48)	28% (88)	<0.001

Current cigarette smoking	14% (n=11)	14% (n=43)	0.91
History of atrial fibrillation or flutter	5% (n=4)	10% (n=32)	0.13
Inpatient status	49% (n=39)	29% (n=90)	0.001
Prior coronary revascularization	62% (n=48)	6% (n=20)	<0.001
Acute myocardial infarction	31% (n=26)	-	-
Body mass index (kg/m^2)	28 (26-33)	28 (24-35)	0.48
Laboratory and CMR characteristics			
Creatinine (mg/dL)	0.9 (0.8-1.2)	0.9 (0.8-1.1)	0.11
Glomerular filtration rate (mL/min/1.73m^2)	82 (62-97)	90 (77-92)	0.20

Ejection fraction (%)	42 (32-59)	59 (50-65)	<0.001
Left ventricular mass index (g/m^2)	63 (52-74)	53 (43-67)	0.001
End diastolic volume index (mL/m2)	92 (73-119)	80 (67-97)	<0.001
Non ischemic or atypical scar evident on LGE images	12% (n=9)	23% (n=71)	0.03

Table 2. Blinded image quality ratings. Image quality ratings were significantly higher for moco-LGE (symmetry statistic 55, p<0.001). The 41 individuals without bh-LGE were excluded

		moco-LGE			
	Frequency (n)	**3 = acceptable**	**4 = good**	**5 = very good**	**Total %**
bh-LGE	**3 = acceptable**	**7**	**42**	**2**	**51** 15%
	4 = good	**5**	**226**	**36**	**267** **77%**
	5 = very good	**0**	**5**	**26**	**31** 9%
	Total %	**12** 3%	**273** 78%	**64** 18%	**349** 100%

Figure Legends

Figure 1. Ten examples of pairs of breath held late gadolinium enhancement (bh-LGE) images and corresponding free-breathing motion-corrected late gadolinium enhancement (moco-LGE) in subjects able to breath hold successfully. Panels A-H depict myocardial infarction; panels I and J show scar in hypertrophic cardiomyopathy and nonischemic cardiomyopathy, respectively (arrows).

Figure 2. In the setting or arrhythmia or inability to breath hold, free-breathing motion-corrected late gadolinium enhancement (moco-LGE) can offer improved image quality compared to breath held late gadolinium enhancement (bh-LGE) images. The patient in panel F had no structural heart disease but did exhibit respiratory motion artifact from chest wall ghosting mimicking mid wall fibrosis on the bh-LGE image that was not present on adjacent slices or moco-LGE images.

Figure 3. We present a case where bh-LGE was not acquired due to atrial fibrillation and inability to breath hold, and moco-LGE revealed opposite results compared to other noninvasive modalities on three critical parameters: ischemia, myocardial infarction (MI), and mural thrombus. A functional 90 year old person had chest discomfort and peak troponins of 4.44 ng/mL. Regadenoson single photon emitted computed tomography (SPECT) revealed no ischemia and a moderate size MI without apparent viability in the left anterior descending artery (LAD) distribution with an apical aneurysm (panel A). Echocardiography also revealed wall motion abnormality in the LAD artery distribution and a “probable” mural thrombus (panel B). Entirely free-breathing CMR also revealed akinetic/aneurysmal wall motion in the LAD distribution. Yet, in contrast to the echocardiogram no thrombus was observed. In contrast to

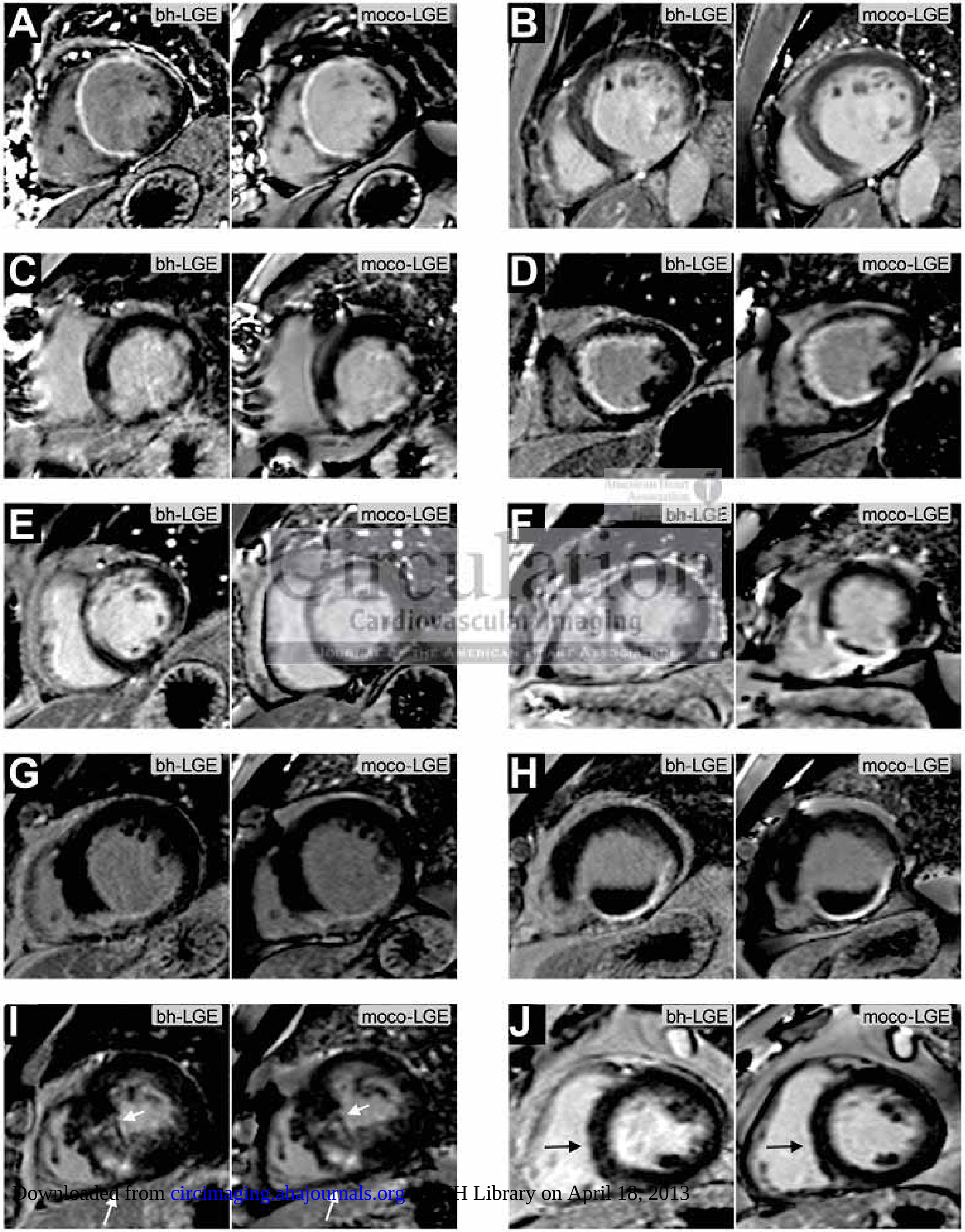
SPECT, no MI was observed in the anterior and anteroseptal walls, rated as entirely viable (panels C and D) using moco-LGE. Given the wall motion abnormality, preserved viability, and lack of history to support stress cardiomyopathy, cardiac catheterization was recommended. We suspected proximal LAD disease with profoundly ischemic stunned or hibernating myocardium, despite the SPECT exam. Based on the moco-LGE data as well as prior data,[30] we predicted full functional recovery if revascularization was feasible. At catheterization, a 90% LAD lesion supplying a large amount of myocardium was stented restoring luminal patency; the procedure was complicated by a small left main dissection. The patient returned for CMR 3 months later; cines exhibited full functional recovery confirming initial LAD territory viability claims by CMR (panels C and D). A tiny apical wall motion abnormality persisted (asterisk, panels E and F). One year later, this patient enjoys a high quality of life without any cardiac complaints or events. (See supplementary material for additional case data).

Figure 4. Free-breathing motion-corrected late gadolinium enhancement (moco-LGE) images are considerably faster to acquire than conventional breath held segmented late gadolinium enhancement (bh-LGE) images in routine CMR practice (n=100).

Figure 5. When bh-LGE image quality was artifact-free, scatter plots and Bland-Altman plots show high correlation and excellent agreement across the myocardial infarction size spectrum without evidence of bias (solid and dotted lines indicate mean difference and ±1.96 SD of the differences, respectively). Infarct mass was measured blindly from stacks of short axis images.

Figure 6. Outcomes examining incident hospitalization for heart failure or death according to bh-LGE or moco-LGE findings. Panel A reveals that vulnerable patients *confirmed by their*

heart failure/mortality outcomes had significantly decreased image quality in proportion to their vulnerability, and those with the worst event-free survival had bh-LGE imaging abandoned altogether (n=41 of 390) by the supervising CMR physician at the time of the clinical scan (thick line). Thus, bh-LGE image quality was inversely related to patient vulnerability (log rank 16.8; p<0.001). Panel B reveals no such relationship between outcomes and moco-LGE image quality (log rank 1.4; p=0.5). Panel C reveals abnormality observed on bh-LGE (n=128 of 349) was not able to achieve statistical significance given the omission of the 41 vulnerable individuals in panel A without bh-LGE image acquisition (log rank. 3.64; p=0.056). Panel D shows that abnormality observed on moco-LGE (n=156 of 390) which included all patients significantly stratified risk on the entire sample (log rank. 6.0; p=0.014).


A
bh-LGE
moco-LGE
B
bh-LGE
moco-LGE
C
bh-LGE
moco-LGE
D
bh-LGE
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E
bh-LGE
moco-LGE
F
bh-LGE
moco-LGE
G
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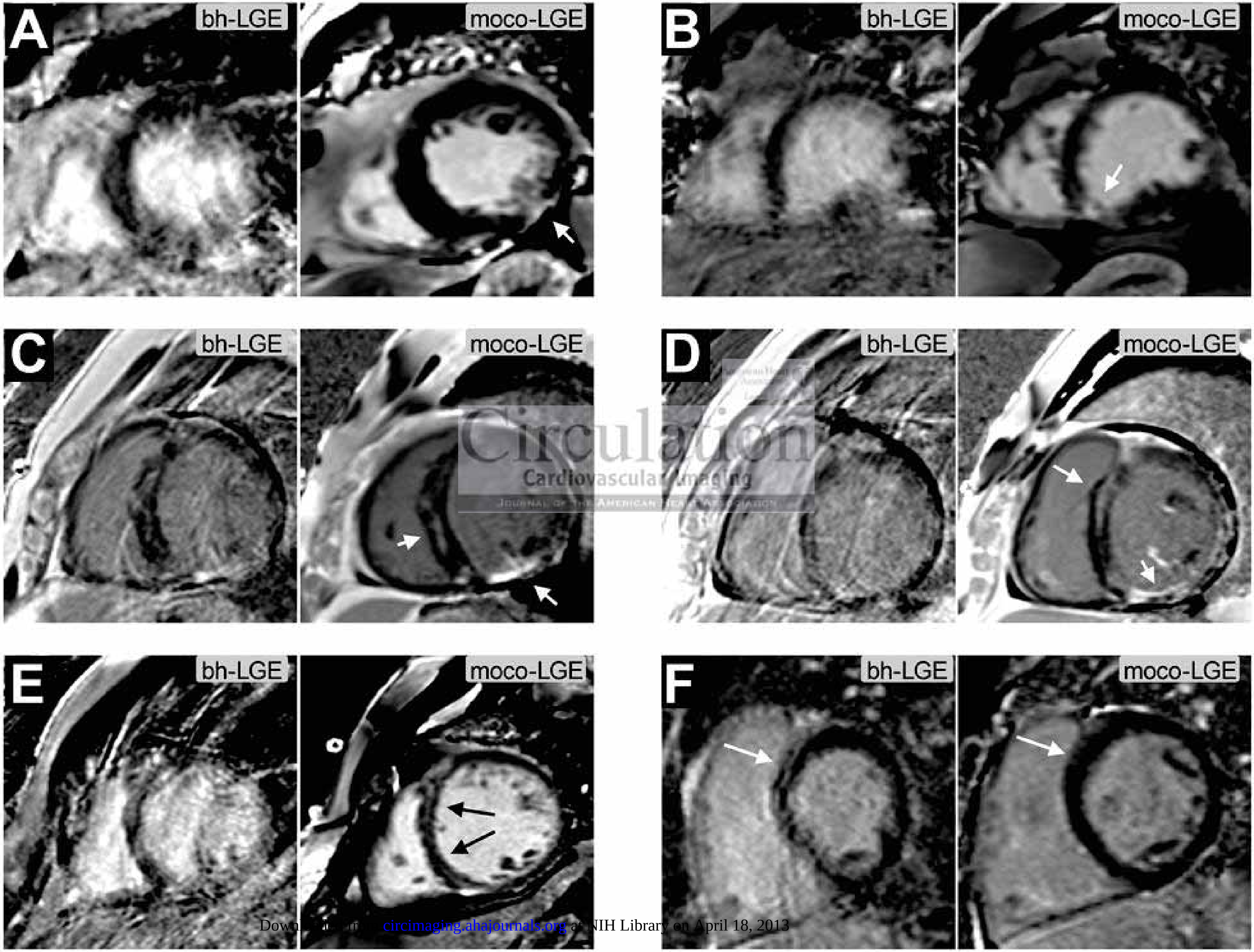
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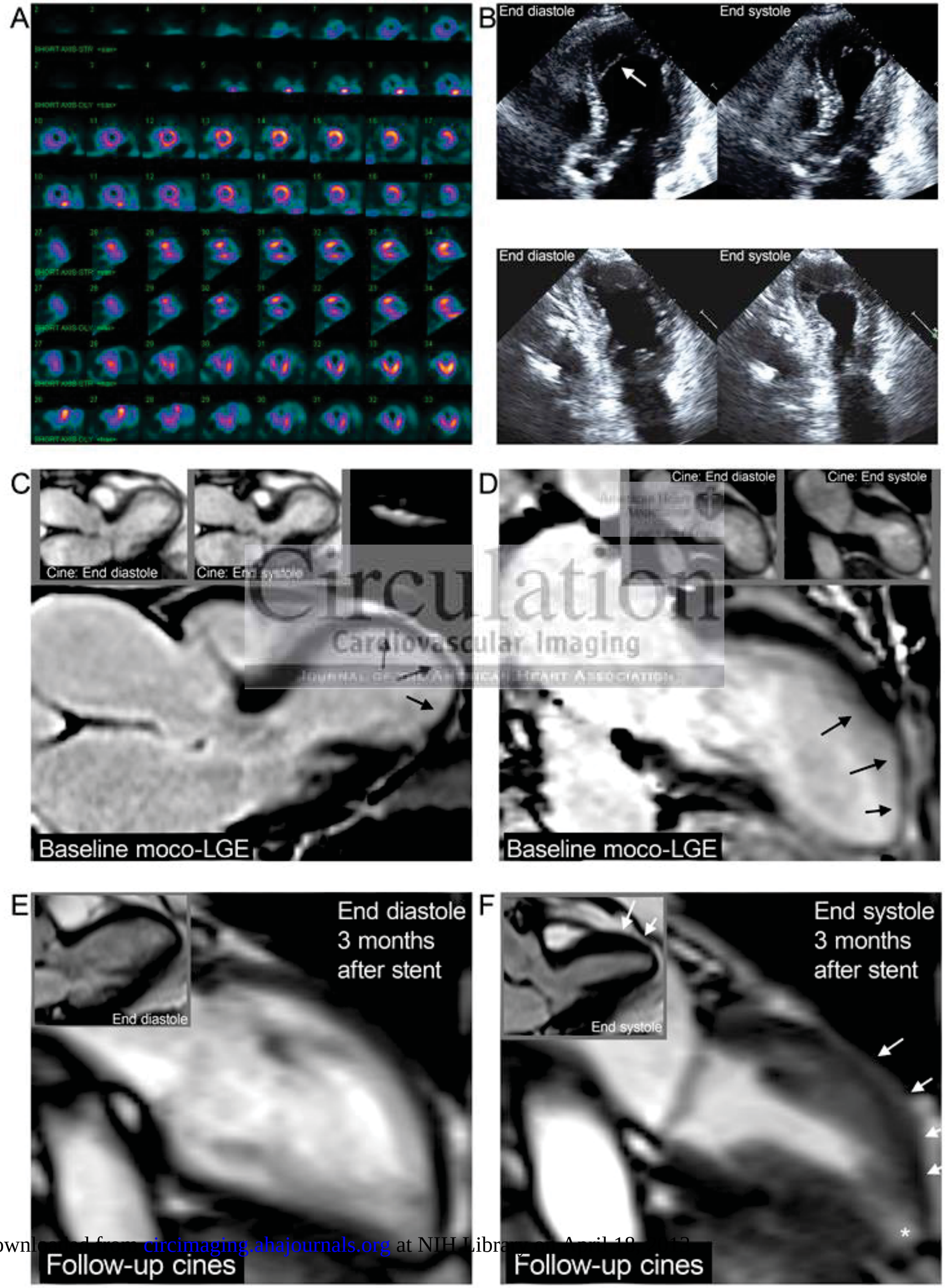
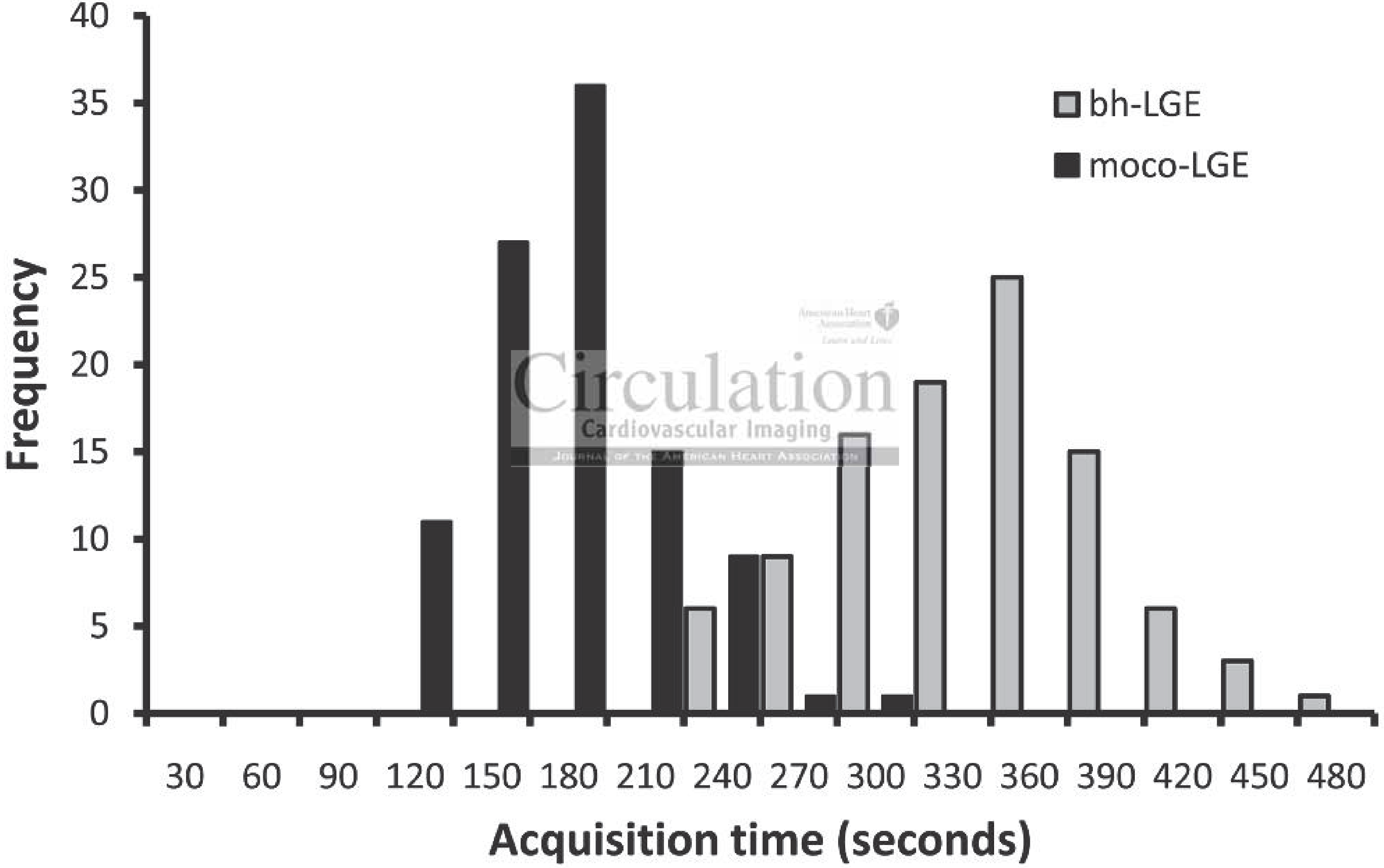
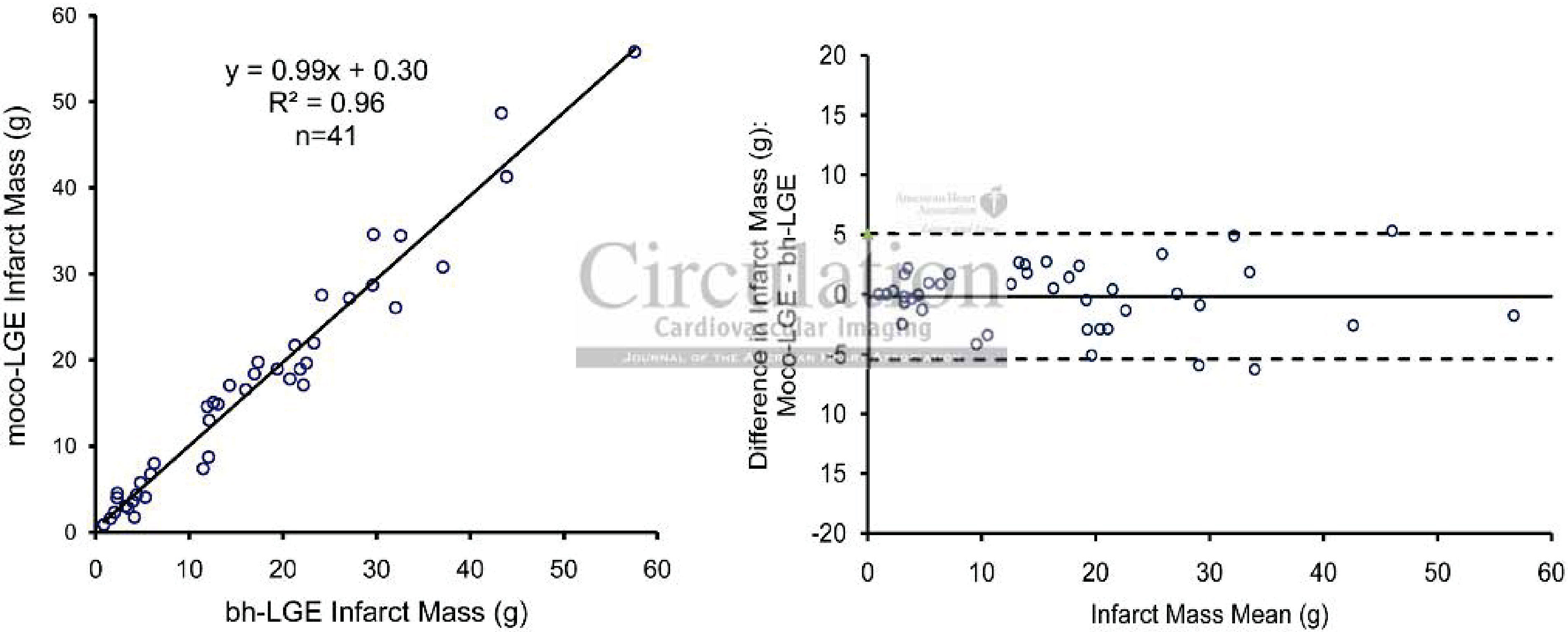

A
B
End diastole
End systole
End diastole
End systole
C
Cine: End diastole
Cine: End systole
Baseline moco-LGE
D
Cine: End diastole
Cine: End systole
Baseline moco-LGE
E
End diastole
3 months
after stent
End diastole
Follow-up cines
F
End systole
3 months
after stent
End systole
Follow-up cines



Frequency
0
5
10
15
20
25
30
35
40
bh-LGE
moco-LGE
30
60
90
120
150
180
210
240
270
300
330
360
390
420
450
480
Acquisition time (seconds)
Circulation
Cardiovascular Imaging
Journal of the American Heart Association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R² = 0.96
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moco-LGE Infarct Mass (g)
bh-LGE Infarct Mass (g)
0
10
20
30
40
50
60
Difference in Infarct Mass (g):
Moco-LGE - bh-LGE
Infarct Mass Mean (g)
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15
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5
0
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10
15
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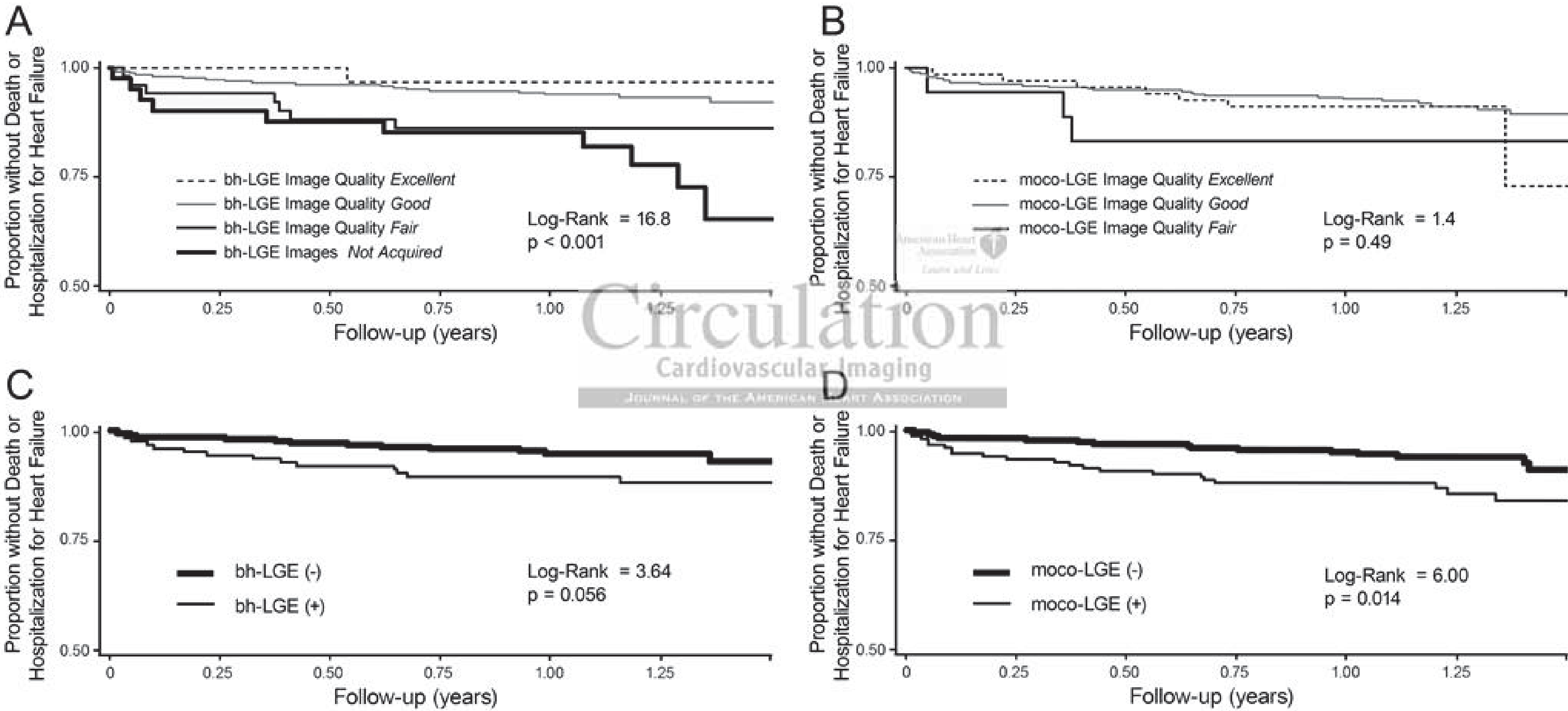


A
Proportion without Death or Hospitalization for Heart Failure
1.00
0.75
0.50
0
0.25
0.50
0.75
1.00
1.25
Follow-up (years)
bh-LGE Image Quality Excellent
bh-LGE Image Quality Good
bh-LGE Image Quality Fair
bh-LGE Images Not Acquired
Log-Rank = 16.8
p < 0.001
B
Proportion without Death or Hospitalization for Heart Failure
moco-LGE Image Quality Excellent
moco-LGE Image Quality Good
moco-LGE Image Quality Fair
Log-Rank = 1.4
p = 0.49
Follow-up (years)
C
Proportion without Death or Hospitalization for Heart Failure
bh-LGE (-)
bh-LGE (+)
Log-Rank = 3.64
p = 0.056
Follow-up (years)
D
Proportion without Death or Hospitalization for Heart Failure
moco-LGE (-)
moco-LGE (+)
Log-Rank = 6.00
p = 0.014
Follow-up (years)

SUPPLEMENTAL MATERIAL

Supplementary Table. Blinded diagnostic confidence ratings. Image confidence ratings were significantly higher for moco-LGE (McNemar's test p=0.02).

		moco-LGE		
	Frequency (n)	**2 = some confidence**	**3 = high confidence**	**Total %**
bh-LGE	**2 = some confidence**	**6**	**26**	**32** 9%
	3 = high confidence	**12**	**305**	**317** 91%
	Total %	**18** 5%	**331** 95%	**349** 100%

Supplementary Video/Figure Legends

Supplementary Video 1. Three chamber cine CMR showing marked wall motion abnormality and corresponding moco-LGE image showing preserved viability upon presentation.

Supplementary Video 2. Four chamber cine CMR showing marked wall motion abnormality and corresponding moco-LGE image showing preserved viability upon presentation.

Supplementary Video 3. Two chamber cine CMR showing marked wall motion abnormality and corresponding moco-LGE image showing preserved viability upon presentation.

Supplementary Video 4. Short axis cine CMR stack showing marked wall motion abnormality and corresponding moco-LGE image showing preserved viability upon presentation.

Supplementary Video 5. Long axis echocardiogram showing possible mural thrombus in the setting of marked wall motion abnormality upon presentation.

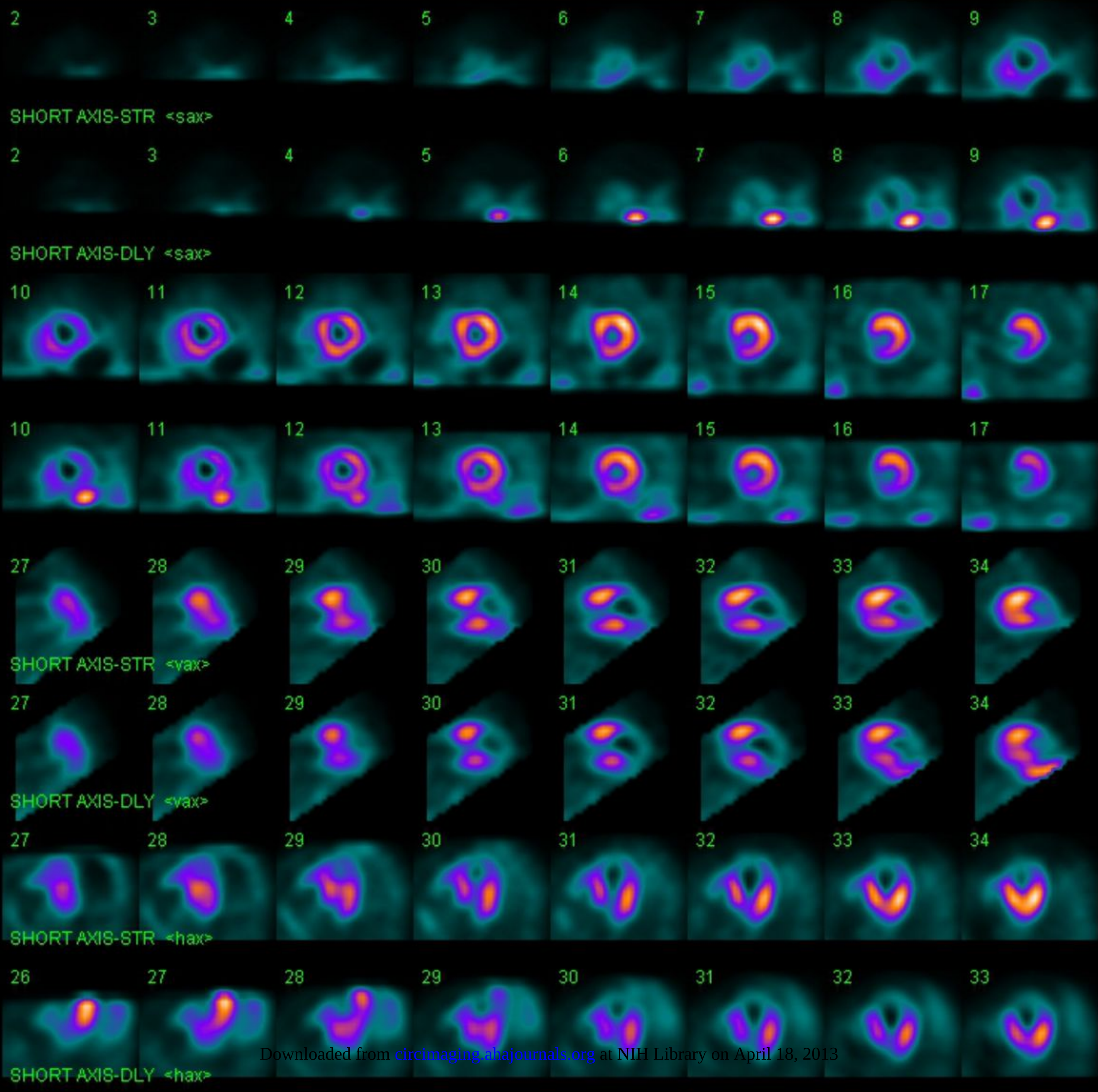
Supplementary Video 6. Coronary cine angiogram of the left anterior descending artery in the left anterior oblique cranial projection showing severely calcified disease with proximal serial stenoses up to 90% and diffuse mid and distal disease.

Supplementary Video 7. Coronary cine angiogram of the left anterior descending artery in the right anterior oblique cranial projection showing severely calcified disease with proximal serial stenoses up to 90% and diffuse mid and distal disease.

Supplementary Video 8. Two chamber cine CMR showing marked improvement in the wall motion abnormality before and 3 months after coronary intervention in the left anterior descending artery.

Supplementary Video 9. Three chamber cine CMR showing marked improvement in the wall motion abnormality before and 3 months after coronary intervention in the left anterior descending artery.

Supplementary Figure. Regadenoson SPECT myocardial perfusion study performed upon presentation showing a) no significant ischemia, b) a resting perfusion abnormality in the anterior apical, apex, inferoapical, apical septum and apical lateral wall, consistent with prior myocardial infarction in the mid left anterior descending coronary artery distribution, and c) an apical aneurysm.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