GADOFOSVESET OPTIMIZATION FOR SELF-NAVIGATED CORONARY MR ANGIOGRAPHY

Mark A Ahlman[1], Scott Penzak[2], Fabio Raman[1], Jianing Pang[3], Songtao Liu[1], Debiao Li[3], and David A Bluemke[1]

[1]Radiology and Imaging Sciences, National Institutes of Health, Bethesda, Maryland, United States, [2]Pharmacy, National Institutes of Health, Bethesda, Maryland, United States, [3]Bioengineering, Cedars-Sianai Medical Center, Los Angeles, California, United States

Target Audience

Scientists and clinicians involved with research of MRA and/or contrast pharmacokinetics of gadolinium based contrast agents (GBCAs).

Purpose

Coronary MRA sequences typically employ real time monitoring of diaphragm motion in tandem with ECG triggering of pulse sequences in order to acquire a motion free diagnostic image of the whole heart. These sequences are lengthy (10-15 min) and require a very cooperative patient. Achieving a short T1 time for such a prolonged interval is impractical with conventional extracellular GBCA agents[1]. Gadofosveset, with its high intravascular residence time compared to other GBCAs, is theoretically well suited for this application. Recently, a protocol was designed in order to employ a free-breathing coronary MRA that affords 100% imaging efficiency without real-time navigator gating[2-3]. For contrast enhanced MRA at 3T, such a sequence may be consistent with an intravascular contrast agent if an injection protocol is designed to achieve a stable and short T1 time. An optimized injection technique for this purpose with Gadofosveset does not currently exist. Here we propose a dual injection protocol to maintain a stable concentration of Gadofosveset for a 5-6 minute MRA acquisition window.

Methods

As an initial step, Gadofosveset plasma concentration vs time profiles were simulated using WinNonlin pharmacokinetic (PK) software, version 5.0 (Pharsight Corporation, Mountain View, CA, USA). Initial PK simulations were obtained from the commercial package insert (Ablavar®, Lantheus Medical Imaging, North Billerica, MA, USA). Modeling parameters focused on simulating a dual phase dosing regimen that produced the least amount of variability in Gadofosveset plasma concentrations if a bolus were followed by a 5-minute continuous infusion. After pharmacokinetic modeling, normal volunteers (no history of heart disease, age <40) for contrast enhanced MRA were selected, screened for MR safety, and signed affirmation of informed consent. Following injection of Gadofosveset using a Spectris Solaris EP (MEDRAD Inc, Pittsburgh, PA, USA) MR injector, 4-chamber single-slice 11-heart beat Modified Look-Locker Inversion Recovery (MOLLI) sequences were acquired in 45-60 second intervals during breath holding on a 3T Verio (Siemens Corp) with body matrix coils. T1 maps were used to measure absolute T1 times in the left ventricle lumen (LV) and basal interventricular septum (Myo) with QMass MR ver 7.2 (Medis, Raleigh, NC, USA). The earliest scanning time point was recorded that visually demonstrated a concentration consistent with an overall steady concentration. A percentage change in T1 time from this early point and up to 5 minutes was recorded. A change in raw T1 times or vascular/myocardium ratios >10% were considered insufficient.

Results

Modeling of PK parameters found that the least variation in intravascular concentration over 5 min (<1.7%) resulted from a 70/30% bolus/infusion split. This ratio was used to program the injector (Table 1). Mean (min-max) values are reported hereafter. Appreciated in Figure 1 (Myo T1 curves on top and LV T1 on bottom), the earliest scanning point that demonstrated a concentration consistent with the overall seady concentration was 83s(63-93) following the beginning of the injection protocol. When this time point is used as the hypothetical beginning of a 5 min acquisition, change in LV T1 time was -4.4%(-2.3 to -5.8) with a Myo T1 time change of -4.1%(-1.8 to -6.7), and a LV/Myo change of +1.3%(-1.1 to +2.7).

Table 1 70%/30% bolus/infusion technique in order to quickly reach steady state intravascular concentration of Gadofosveset followed by maintainence of concentration for 5-6 minutes.

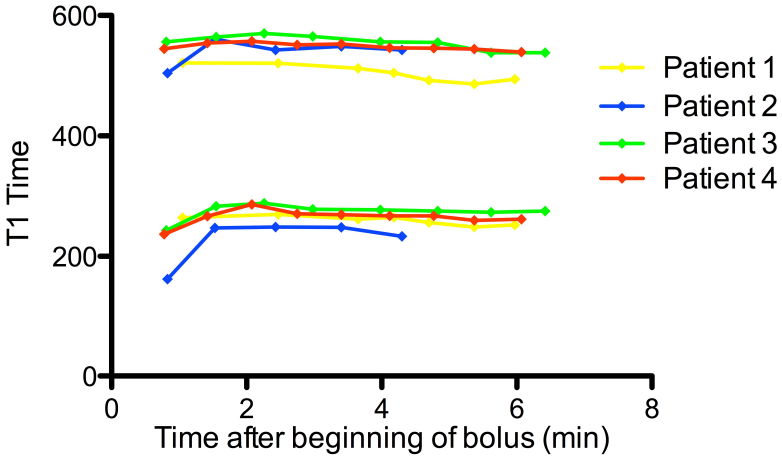
Prior to scan	Vial A	50ml of saline/Gadofosveset mixed uniformly
	Vial B	42ml of saline + 8ml saline in line = 50ml
Bolus dose (70% of contrast)	Vial A	35ml @ 3ml/sec (11.6 sec bolus)
	Vial B	20ml @ 3ml/sec (4.0 sec bolus)
	Vial A	8ml @3ml/sec (2.6 sec line primer)
		*PAUSE 45 seconds
		*START SCANNING
		*PAUSE 45 seconds
Infusion dose (30% of contrast)	Vial A	8 ml @ 0.06 ml/sec for 2.22 min
	Vial B	10 ml @ 0.06 ml/sec for 2.77 min

*Subject to experimental variation

Discussion

There is stable concentration during the proposed 5-6 minute acquisition duration for all T1 parameters measured (LV, Myo, LV/Myo). The starting scan time is 60-90 seconds after the beginning of the injection. We found the injection schema to be easy to use, affords low risk of complications because of mild flow rate (max 3ml/s), and were well tolerated by volunteers.

Figure 1 Minutes after bolus vs T1 time



Conclusion

We proposed and validated a mathematically derived injection protocol for an intravascular contrast agent (Gadofosveset) that results in near constant blood T1 time over 5-6 minutes. Such an injection protocol should be the idea for a 3D radial coronary MRA sequence with self-navigation[2-3]. Using this model, we give evidence for proof-of-concept of the clinical applicability of our injection technique in humans.

References

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