Theoretical Limits of Spatial Resolution in Elliptical-Centric Contrast-Enhanced 3D-MRA

Sean B. Fain, Stephen J. Riederer,* Matt A. Bernstein, and John Huston III

The point spread function (PSF) for contrast-enhanced three-dimensional (3D) MR angiography using the elliptical centric view order is derived. This view order has been shown previously to provide high venous suppression thereby enabling long acquisition times capable of high spatial resolution. The dependence of the PSF on TR, field of view (FOV), scan time, and trigger time are shown explicitly. Theoretical predictions are corroborated with experimental results in phantoms and in vivo. The PSF width decreases as the square root of the product of TR and the two phase encoding FOV’s for fixed nominal voxel size. The PSF peak amplitude increases as the reciprocal of this product. Theory and experiment demonstrate that acquisition times over 40 sec provide superior resolution compared to shorter acquisitions, despite falling levels of contrast agent concentration. The analysis predicts that an isotropic spatial resolution of 1 mm before zero filling is possible in a FOV large enough to encompass the carotid and vertebral arteries bilaterally. Magn Reson Med 42:1106–1116, 1999. © 1999 Wiley-Liss, Inc.

Key words: MR angiography; contrast-enhanced MRA; point spread function; elliptical centric view order

Three-dimensional contrast-enhanced magnetic resonance angiography (3D CE-MRA) using intravenously injected Gadolinium (Gd) contrast agent is a rapidly gaining acceptance as an effective technique for visualization of the vascular system (1–3). Compared to X-ray angiography, however, the spatial resolution of this technique is still limited. Blurring principally stems from the changing concentration of the contrast material within the targetted vasculature, and from motion during the 3D acquisition. The purpose of this work is to show rigorously how the dynamic nature of the contrast bolus, as mapped to 3D -space during the data acquisition, imposes limitations on the spatial resolution and signal level attainable in 3D CE-MRA. The analysis can guide selection of image acquisition parameters, including the scan time, in order to obtain the highest possible resolution and signal for a given contrast bolus profile.

The specific topic of this work, resolution limits in contrast-enhanced MR angiography, is related to the more general topic of resolution limits in MRI as imposed by the transient or nonconstant nature of the magnetization in specific pulse sequences. Examples which have been studied previously include the resolution limits imposed by $T_2^*$ decay in echo-planar imaging (4), by $T_2$ decay in RARE spin-echo imaging (5), and by $T_2^*$ decay in high resolution MR microscopy (6). In each of these cases it is the dynamic nature of the relevant physical phenomenon that imposes the ultimate limit to spatial resolution.

That the dynamic contrast bolus is now the factor that limits spatial resolution in 3D CE MRA can be seen by tracing the evolution of this technique. As initially implemented (7–9), the contrast infusion and imaging times were several minutes long. These long times resulted in unacceptably high venous signal, as well as the potential for significant motion artifacts. To address these major deficiencies, imaging of the first arterial pass of the administered contrast agent was developed, but this raised new problems, most notably timing of the acquisition to the contrast bolus (10–18), and limited spatial resolution. One way to address the timing issue is by time-resolved imaging, with 3D acquisition times typically in the 5–10 sec range (3,18), possibly in conjunction with view sharing (19). Because these methods use data from only a portion of the duration of the contrast bolus to form a single image, they have limited spatial resolution (20). Others have addressed the bolus timing issue by administering a test bolus to estimate arrival time (14,21,22), or by using real-time techniques such as line scan methods (23,24), or two-dimensional (2D) fluoroscopic monitoring (25,26) to trigger the 3D scan. Time-resolved and triggered methods have been used successfully, and in both cases the central k-space views are acquired during the arterial phase of the contrast bolus. The real-time triggered methods all use a centric view order, in which the central views are acquired at the outset of the acquisition, which is synchronized to the peak arterial phase. Specifically, an “elliptical centric” view order (27) which is centric in both phase encoding directions provides very high venous suppression in imaging of the renal (25) and carotid arteries (28) even with acquisition times of the latter exceeding 40 sec. To summarize, a common or triggered elliptical centric method permits extended acquisition times and high resolution, while still providing high venous suppression. Because the problem of venous suppression has been addressed, the question of bounds on spatial resolution due to the shape of the contrast bolus becomes relevant.

In the next sections we model the temporal characteristics of bolus profiles in 3D CE MR angiography, derive an analytical expression of the point spread function (PSF) given an elliptical centric view order, and test and discuss implications of the result. As a specific clinical application we target imaging of the carotid and vertebral arteries bilaterally, and show that 1 mm isotropic spatial resolution before zero filling is possible.
METHODS

Theory

Measurement and Modeling of In Vivo Bolus Profiles

A critical element in determining spatial resolution is the temporal shape of the bolus profile. In order to observe the range of enhancement behavior in patients, nine in vivo enhancement curves in as many patients were measured. Two-dimensional complex subtraction images were generated at a rate of 1 image/sec for an oblique sagittal plane positioned to include the left common carotid artery and jugular vein longitudinally. For all cases, the same injection technique was used: 20 ml Gadoteridol (Prohance, Bracco Diagnostics, Princeton, NJ) was administered at 3 ml/sec into the right antecubital vein, followed by a 20 ml saline flush injected at 2 ml/sec. The value of the maximum intensity pixel within each vessel was sampled for each image to reconstruct the contrast enhancement profile.

Next, the measured arterial bolus curves were fitted to various mathematical expressions based on gamma-variate functions (29). The measured curves all had a first pass or arterial enhancement phase, and the first fit considered was a single gamma-variate of the form:

\[ b(t) = kt^n e^{-\tau t}, \quad [1] \]

where \( k \), \( n \) (possibly noninteger) and \( \tau \) are all fitted parameters and \( t \geq 0 \). The fits sought to minimize the least square error, \( \chi^2 \), between the measured data and the fitted function. The reduced \( \chi^2 \), or \( \chi^2_o \), is the \( \chi^2 \) normalized to the degrees of freedom in the fit. When \( \chi^2 \) approaches one, the fitting function is considered to be a good approximation to the data (30). The \( \chi^2_o \) for the single gamma-variate, Eq. [1], was considerably greater than unity (Table 1), so this model was abandoned.

Each measured curve had a residual enhancement phase that persisted for at least 40 to 50 sec after the first pass, peaking at 25 to 40% of the maximum first pass enhancement and then gradually decaying (Fig. 1a). It is this residual component which represents a major deviation from a single gamma-variate model in Eq. [1]. The observed two-phase behavior of the in vivo curves were then fitted to a sum of two gamma-variates, the first mimicking the initial arterial phase and the second the residual contrast. To simplify the analysis, the arrival time of the residual gamma-variate was assumed to occur at the peak time of the first pass curve. Although the PSF can be analytically determined by Fourier transformation of a gamma-variate function (Eq. [1]) where \( n \) is an arbitrary integer, the mathematical expression increases in complexity, and the intuitive interpretation becomes less obvious as \( n \) increases. Therefore, in the initial two-phase model, both the arterial and residual gamma-variates were constrained to have \( n = 1 \). This led to some reduction in \( \chi^2 \) (Table 1), but the fitted curve was still not an adequate representation of the measured data.

![FIG. 1.](image)

**Table 1**

<table>
<thead>
<tr>
<th>Model tested</th>
<th>Mean ( \chi^2_o ) ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single phase, fitted ( n )</td>
<td>5.3 ± 5.1</td>
</tr>
<tr>
<td>Two phase, ( n = 1 )</td>
<td>4.3 ± 3.2</td>
</tr>
<tr>
<td>Two phase, ( n = 2 )</td>
<td>0.9 ± 0.4</td>
</tr>
</tbody>
</table>

The measured enhancement curve shown in (a) is used for the experiments in this paper \( \tau_1 = 4.7 \) sec, \( \tau_2 = 21.3 \) sec, \( C_R = 0.37 \), where \( C_R \) is defined as the ratio of the peaks of \( b_2(t) \) to \( b_1(t) \).
Next the two-phase model was considered with \( n = 2 \). Noting that an \( n = 2 \) gamma-variate peaks at \( t = 2\tau \), and locating the time origin at the peak of the first gamma-variate, we obtain, as developed in the Appendix:

\[
\text{b}(t) = b_0(t) + b_2(t) \quad [2a]
\]

where \( \tau_1 \) and \( \tau_2 \) are the fitted characteristic time constants and \( c_1, \tau_1^2 \) and \( c_2, \tau_2^2 \) are the fitted relative peak amplitudes of the arterial first pass, \( b_0(t) \), and residual curves, \( b_2(t) \), respectively. These values are reported for each of the fitted curves in Table 2.

Selection of the time origin of \( b(t) \) to be equal to the time of the peak of the arterial phase curve \( b_0(t) \) is equivalent to assuming that the 3D acquisition is triggered at the peak of the first arterial pass. Triggering at or near this time is routinely possible with fluoroscopic triggering (26,28).

The \( x_2^2 \) value for Eq. \( [2b] \) was near unity as desired (Table 1), and so this two phase model was used for all subsequent analysis in this work. To illustrate various aspects of this analysis, we chose a representative measured curve, shown in Fig. 1a along with its fitted profiles

\[
\tau_1 = 4.7 \text{ sec}, \quad \tau_2 = 21.4 \text{ sec}, \quad C_R = \frac{c_2}{c_1} = \frac{\tau_2^2}{\tau_1^2} = 0.37.
\]

Point Spread Function (PSF) of the Composite Bolus Profile

The PSF of the composite bolus profile is derived by first converting the time dependence of \( b(t) \) to a k-space-dependent modulation, and then performing the inverse Fourier transformation. Such a derivation for a single gamma-variate is done in the Appendix. Noting that subscripts “1” and “2” denote the arterial and residual curves, respectively, and using Eqs. [A10b] and [A7], the k-space modulation \( H(k) \) due to the composite gamma-variate of Eq. [2] is given by

\[
H(k) = H_1(k) + H_2(k) \quad [3a]
\]

where

\[
M = \frac{\Delta k_2 \cdot \Delta k_2}{\text{TR}} = (\text{FOV}_y \cdot \text{FOV}_z \cdot \text{TR})^{-1}, \quad [3c]
\]

and \( k \) is the radial k-space variable, and \( C_R \) is the ratio of the peak residual contrast curve to the peak of the first pass contrast curve. The k-space dependence, \( H(k) \), is shown for a trigger time at peak enhancement (Fig. 1b) for the sample contrast enhancement curve shown in Fig. 1a. The Hankel transform of Eq. [3b] then results in the PSF, \( h(r) \), of the composite profile (Fig. 1c). Using Eq. [A9] with \( l = \tau_2/\tau_1 \):

\[
\frac{1}{2} h(0) = \frac{1}{2} M |5e^{-2} + 1 \cdot C_R| = \frac{|5e^{-2} + 1 \cdot C_R|}{2TR \cdot \text{FOV}_y \cdot \text{FOV}_z} = h(r_{1/2}). \quad [5]
\]

Solving for \( r_{1/2} \) is facilitated by defining the dimensionless variable, \( u = \pi M \tau_1 \tau_2^2/2 \). This yields

\[
\frac{1}{2} |5e^{-2} + 1 \cdot C_R| = e^{-2u} \cdot [5 - 4u + \frac{\pi^2}{2}] + 1 \cdot C_R e^{-u^2} \cdot [1 - 2(u + \frac{\pi^2}{2})]. \quad [6]
\]

Now \( u \) is solved for numerically. For the specific values of \( l = \tau_2/\tau_1 = 4.6 \) and \( C_R = 0.37 \), which characterize the sample bolus profile of this work, \( u = 0.646 \) and thus:

\[
\text{FWHM} = 2\sqrt{\frac{\text{TR} \cdot \text{FOV}_y \cdot \text{FOV}_z}{\pi \cdot \tau_1}} \cdot 0.064. \quad [7]
\]

This result expresses the fundamental square root dependence of FWHM on the major acquisition parameters TR, FOV\(_y\), and FOV\(_z\) and the time constant \( \tau_1 \) of the first pass arterial contrast phase.

PSF Dependence on Scan Time

The analytical solution to the PSF for the gamma-variate profile Eq. [2b] assumes an infinite scan time. For finite scan times, the PSF is calculated by multiplying \( H(k) \), Eq. [3], by a cylindrical \text{rect} window function (31), and then Fourier transforming the result. Thus, data up to the k-space radius representing the desired scan time are preserved, while zeros are applied to all larger k values.

Table 2
Fitted Parameters for Measured Curves

<table>
<thead>
<tr>
<th>Patient</th>
<th>( \tau_1 ) (sec)</th>
<th>( \tau_2 ) (sec)</th>
<th>( C_R )</th>
<th>( x_2^2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.85</td>
<td>12.5</td>
<td>0.23</td>
<td>0.5</td>
</tr>
<tr>
<td>2</td>
<td>3.15</td>
<td>10.2</td>
<td>0.24</td>
<td>1.3</td>
</tr>
<tr>
<td>3</td>
<td>3.25</td>
<td>13.7</td>
<td>0.25</td>
<td>1.0</td>
</tr>
<tr>
<td>4</td>
<td>3.15</td>
<td>16.4</td>
<td>0.37</td>
<td>0.9</td>
</tr>
<tr>
<td>5</td>
<td>3.50</td>
<td>17.5</td>
<td>0.30</td>
<td>0.9</td>
</tr>
<tr>
<td>6</td>
<td>4.70</td>
<td>21.4</td>
<td>0.37</td>
<td>0.8</td>
</tr>
<tr>
<td>7</td>
<td>5.45</td>
<td>23.7</td>
<td>0.40</td>
<td>1.2</td>
</tr>
<tr>
<td>8</td>
<td>4.05</td>
<td>12.2</td>
<td>0.29</td>
<td>0.6</td>
</tr>
<tr>
<td>9</td>
<td>4.25</td>
<td>19.8</td>
<td>0.47</td>
<td>1.5</td>
</tr>
</tbody>
</table>

\(^{a}C_R \) is defined as the ratio of the peaks of \( b_2(t) \) to \( b_1(t) \).
This was done numerically for a range of k-space radii representing scan times from 10 to 230 sec, and the resulting PSF’s were compared to the theoretical PSF for an infinite scan time.

Determination of the maximal useful scan duration depends on the duration of useful contrast enhancement. One criterion for the spatial resolution limit is to set the nominal pixel size to be just finer than the blurring due to the PSF. By the Rayleigh criterion adjacent line pairs become indistinguishable if their spacing is just less than one-half the FWHM of the PSF (32). Starting with Eq. [7] and using this criterion (i.e., $\text{FOV}_y/\text{Ny} = \text{FOV}_y/N_z = 1/2$ FWHM), the scan time $T_{\text{scan}} = T_R \cdot N_y \cdot N_z$ beyond which no gain in spatial resolution can be expected is

$$T_{\text{scan}} = \frac{\pi \cdot \tau_1}{u(1, C_k)}.$$  

[8]

For the sample bolus profile considered in this work, $T_{\text{scan}}$ computed in this way is 230 sec.

PSF Dependence on Trigger Time

It has been assumed thus far that the 3D acquisition is triggered precisely at the peak of the arterial phase of the contrast bolus. As defined in Eq. [A2], the term $f$ represents the trigger time relative to the arrival time of the contrast bolus expressed in units of the time constant $\tau$. Equation [2b] assumes both triggering and arrival of the residual phase occur at the peak of the arterial phase [i.e., $f_1 = 2$ for $b_1(t)$ and $f_2 = 0$ for $b_2(t)$]. However, the analysis permits arbitrary values of $f$, and alternative triggering times can be studied by adjustment of these $f$ values.

First consider a trigger time $T$ later than the peak of the arterial phase: $T = T_1$, with $f_1 \geq 2$. The specific value for the delay $f_2$ for the residual phase is determined from the elapsed time after the peak of arterial phase:

$$T - 2 \tau_1 = f_2 \cdot \tau_2.$$  

[9]

Using the above definition of $T$ and solving for $f_2$ gives

$$f_2 = (f_1 - 2) \cdot (\tau_1/\tau_2).$$  

[10]

Thus, for triggering after peak, well-defined values of $f_1$ and $f_2$ can be inserted into the corresponding expressions for $b_1(t)$ and $b_2(t)$, and the closed form solution of $h(r)$ determined.

For triggering before the peak, i.e., $0 < f_1 < 2$, the analysis requires additional attention. Specifically, the mathematical function describing the residual contrast phase is nonzero for times preceding the time origin of the residual phase, but physically this function should be zero in this region. This can be addressed by adding a correction term to the composite bolus profile

$$b(t) = b_0(t) + b_1(t) - Ke^{-\pi t}$$  

[11]

where $K$ and $s$ are determined by Taylor series expansion of the residual bolus profile $b_0(t)$ over the problematic time interval. This gives

$$K = l \cdot C_k \cdot e^{-5b} \cdot (f_2/2\tau_2)$$  

[12a]

$$s = (2/5\tau_2) \cdot (1 - f_2/2)$$  

[12b]

For brevity we omit the corresponding derivation, but note that the resultant expression models the desired situation with an error less than 5% of the peak bolus signal for trigger times as early as one time constant $\tau$ prior to peak for the most extreme of the measured bolus profiles.

Determination of some “optimal” trigger time is subjective, as there are several phenomena to consider. First, as trigger time is delayed after contrast arrival, the portion of the contrast bolus used for image formation is diminished, and overall signal is undesirably reduced. However, as trigger time is advanced prior to the time of peak contrast there is edge enhancement, as also seen with sequential and other centric view orders (33). We attempt to define an optimum as follows. First, the peak signal, $h(0)$, was determined as a function of the triggering time. Second, the net area of the PSF, $h(r)$, was also determined as a function of the trigger time. The larger this area, then the larger is the difference in areas between the positive portion of $h(r)$ and the undesirable negative side lobes, which reflect edge enhancement. By the Fourier integral theorem, the total area of $h(r)$ is equal to $H(0)$. Using these quantities a figure-of-merit (FOM), dependent on the trigger time $f_1$, was defined as

$$\text{FOM}(f_1) = \frac{h(0, f_1)}{H(0, f_1)} + \frac{H(0, f_1) - H(0, f_1 = 2)}{H(0, f_1 = 2)}.$$  

[13]

The first term depends on the peak value of the PSF; signal in the image increases as this term increases. The second term depends on the relative positive to negative area of the PSF; edge enhancement decreases as this term increases.

We reiterate that this definition of the FOM is arbitrary and could be adjusted if, for example, one were more tolerant of edge enhancement. Finally, the FWHM, reflecting the spatial resolution, was also determined as a function of trigger time. All of the above analysis was performed for the sample measured bolus profile for the acquisition parameters $TR = 6.5$ msec, $\text{FOV}_y = 15$ cm, and $\text{FOV}_z = 6$ cm.

Experiments

The expression for the PSF, Eq. [4], was studied to assess the dependence on TR and FOV. Additionally, the theoretical predictions of the PSF result were tested in two types of experiments. The first type, “signal modulation,” was designed to evaluate the effect of different bolus profiles and scan parameters on resolution. The second type, “zero replacement,” was designed to test the effect of a finite scan time on the final PSF.

To perform the signal modulation experiment, a resolution phantom was imaged at high nominal spatial resolutions of 0.5 mm square and 0.8 mm square in the two phase encode ($y$ and $z$) directions. The resolution phantom consisted of nine sets of channels cut into acrylic plastic in sets of five adjacent line pairs at spacings ranging from 0.5
to 3.3 mm and filled with water containing CuSO\textsubscript{4} in solution. The raw k-space data of the phantom was then modulated using the representative bolus curve at the desired imaging parameters, and the phantom image was reconstructed.

Zero replacement exactly mimics the effect of reducing the scan time since the elliptical centric view order samples \(k_x\)-\(k_z\) at progressively larger radii. The acquired raw data from phantom and contrast-enhanced 3D MR angiograms were replaced with zeros starting from the last acquired views according to the reverse of the elliptical centric view order. Fractions of \(\frac{1}{4}\), \(\frac{1}{2}\), and \(\frac{3}{4}\) of the sampled data were zero replaced, thereby modeling scans reduced in duration by these fractions.

The phantom images were acquired with a 1.5 T GE Signa MR (Milwaukee, WI) scanner using a fast 3D SPGR sequence. Imaging parameters were flip angle 20°, bandwidth \(\pm 15.6\) kHz, TR 30 msec, and TE 2.2 msec (\(\frac{5}{8}\) partial echo). The matrix size varied with the desired resolution but ranged from 160 (frequency encode; \(X\)) \(\times\) 190–256 (in-plane phase encode; \(Y\)) \(\times\) 60–128 (slices; \(Z\)). The filtered raw data were reconstructed using homodyne detection (34) in the frequency encode direction. The final image presented was a “slice” perpendicular to the frequency encode direction so that both phase encode directions were represented. Zero-padding was used to increase matrix size for presentation. The high resolution raw data were acquired for two different FOV combinations, each expressed as \(Y\) \(\times\) \(Z\) (in cm): (i) 20 cm \(\times\) 6 cm compared to 15 cm \(\times\) 6 cm at 0.8 mm sampling resolution, (ii) 13 cm \(\times\) 6.4 cm compared to 13 cm \(\times\) 4.0 cm at 0.5 mm sampling resolution.

To further illustrate effects of scan time, zero replacement was also done on raw data from an MR angiogram of the vertebral and carotid arteries of a patient acquired with a 1.5 T GE Signa MR scanner using the same 3D SPGR sequence. Imaging parameters were flip angle 30°, bandwidth \(\pm 32\) kHz, TR 6.5 msec, TE 1.4 msec (\(\frac{5}{8}\) partial echo) with an acquisition matrix size of 160 \(\times\) 168 \(\times\) 38 (\(X\) \(\times\) \(Y\) \(\times\) \(Z\)) reconstructed to 512 \(\times\) 384 \(\times\) 72, and FOV of 20 cm (\(S/I\)) \(\times\) 15 cm (R/L) \(\times\) 5.3 cm (A/P).

RESULTS

TR Dependence

The theoretical k-space weighting and associated PSFs for TRs 4.5, 6.5 and 9 msec are shown in Fig. 2a and b for FOV\(_x\) = 15 cm and FOV\(_z\) = 6 cm. Note that the PSF peak amplitude and FWHM both improve for decreased TR. The FWHM of the PSF decreases as the square root of TR in Eq. [7], while the peak amplitude increases with the reciprocal of TR in Eq. [5]. For the specific case of TR = 4.5 msec, the FWHM is 0.84 mm (Fig. 2b). The 44% decrease in TR from 6.5 to 4.5 msec results in a 17% decrease in FWHM and a 44% increase in the PSF peak.

FOV Dependence

As seen from Eq. [3c] and Eq. [7], the two phase encoded FOVs each play an equivalent role in the PSF as the TR. To illustrate the PSF result, consider a \(Y\) \(\times\) \(Z\) FOV of 20 cm \(\times\) 6 cm. This might be used for imaging the carotid and vertebral arteries bilaterally, with \(Y\) chosen as the R/L direction and \(Z\) taken as A/P. The frequency direction \(X\) is typically chosen as S/I. With this FOV, a TR of 6.5 msec, and assuming the sample bolus curve, the FWHM of 1.2 mm (Fig. 3a). The model predicts that decreasing this FOV to 15 cm \(\times\) 6 cm, while keeping the voxel size fixed, to more tightly include the carotid and vertebral arteries bilaterally will provide a 13% decrease in FWHM and a one-third increase in the PSF peak (Fig. 3a). Finally, consider a reduction to a 13 cm \(\times\) 4 cm coronal slab, enough to cover the carotid bifurcations bilaterally; this yields a 30% decrease in FWHM and a greater than 50% increase in PSF peak compared to the large 20 cm \(\times\) 6 cm FOV first considered. These examples assume an infinite scan time.

The signal modulation experiments corroborate further that these seemingly small FOV changes can have marked effects on attainable spatial resolution. For a FOV reduction purely in the \(Y\) phase encode direction from 20 cm \(\times\) 6 cm to 15 cm \(\times\) 6 cm, presented in Fig. 3b and c, spatial resolution is visibly improved for line pair periods of less.
than 2 mm (Fig. 3b). Similarly, for a FOV reduction purely in Z from 13 cm × 6.4 cm to 13 cm × 4.0 cm (Fig. 3d and e), spatial resolution is visibly improved in the Y direction for line pair periods of less than 1.6 mm (Fig. 3d). This resolution improvement along Y for FOV reduction along Z is a consequence of the isotropy of spatial resolution that stems from the elliptical centric view order’s accounting for FOV differences in the phase encoding directions.

Scan Time Dependence

The PSF’s show decreased FWHM and increased peak amplitudes as scan time increases (Fig. 4a). These PSF’s are calculated for a TR of 6.5 msec and 15 cm × 6 cm FOV. Substantial improvements occur for scan times approaching 1 min or longer, although improvements accrue throughout the acquisition. As the total scan time approaches $T_{\text{scan}} = 230$ sec as defined in Eq. (8), the PSF approaches the PSF for an infinite scan time, as predicted. Zero replacement experiments performed on the modulated raw data of the resolution phantom also show visible gains in spatial resolution and signal as acquisition time is progressively increased (Fig. 4b–e). Zero padded reconstruction kept the display voxel size constant for the scan time experiment. Unlike the FOV and TR dependence experi-

![Graph showing dependence of PSF on FOV](image)

**FIG. 3.** a: PSF for various phase encoding fields of view assuming a TR of 6.5 msec and an infinite scan time. The sample bolus profile was used. b–e: Results of signal modulation experiments for different FOV combinations, with bolus parameters and other acquisition parameters fixed. The distance per line pair, or period, is indicated for each column. Resolution is seen to improve in the Y direction for decreased FOV, (b vs. c) and decreased FOV, (d vs. e).

![Graph showing dependence of PSF on scan time](image)

**FIG. 4.** a: PSF for various scan times showing increased peak and reduced FWHM with increased time. The sample bolus profile was used with TR 6.5 msec and Y × Z FOV of 15 × 6 cm. The corresponding zero-replacement experiments for the resolution phantom (b–e) corroborate the theoretical PSF calculations; the period in millimeters for each line pair is specified in b. As observed for FOV reduction, the resolution of the line pairs is lost when the FWHM of the PSF is approximately equal to the line pair period.
ments, however, the acquisition voxel size is changed by zero replacement since the maximal net k-space radius of nonzero data is reduced.

Further corroboration of resolution improvement for increased scan time is shown in Fig. 5. Figure 5a shows the coronal MIP of the full image set, obtained with an acquisition time of 44 sec. We note parenthetically the virtually complete absence of venous signal. Targeted projections of the diseased left internal carotid artery, reconstructed using zero-replacement for scan durations from 11 to 44 sec (Fig. 5b–e), verify improvements in vessel signal and spatial resolution in the region of the stenosis with increased scan time (Fig. 5b–e, arrow). The resolution obtained with the increasing scan duration approaches that of the X-ray angiogram (Fig. 5f).

Trigger Time Dependence
Figure 6 shows the PSF’s for three discrete trigger times: \( f = 0 \) (contrast arrival), \( f = 2 \) (peak time), and \( f = 3 \) (time \( t_1 \) after peak). Although the FWHM remains relatively constant, edge enhancement and signal loss due to early and late trigger times respectively, visibly degrade image quality (Fig. 6b–d) as expected (33). Figure 7a–d show the PSF peak (Fig. 7a), net PSF positive area (Fig. 7b), FWHM (Fig. 7c), and Figure-of-Merit (Fig. 7d), all as a function of the trigger time \( f_1 \). The maximum of the FOM (Eq. (13)) occurs at \( f_1 = 1.9 \ t_1 \), or just prior to peak contrast at \( f_1 = 2 \). A “triggering window” is shown as a shaded region within which the FOM is within 5% of its maximal value. The width of this region, approximately \( t_1 \), indicates that near-optimal performance is provided by a broad range of trigger times, although later times are prone to venous signal.

DISCUSSION
We have derived an expression for the point spread function (PSF) for the elliptical centric view order, given measured bolus profiles in 3D CE MR angiography. The result quantitatively relates the TR, FOV, trigger time, and bolus profile characteristics to the maximal attainable spatial resolution for this view order. The effect of an arbitrary acquisition time can be calculated exactly by windowing the k-space weighting derived for the infinite acquisition time. For example, with use of a field of view to include the cervical carotid and vertebral arteries bilaterally (20 cm \( \times \) 15 cm \( \times \) 6 cm), TR 6.5 msec, and the sample first pass bolus \( T_1 \) of 4.7 sec, then the FWHM is 1.0 mm. The fundamental dependencies of the analysis are corroborated by experiments.

Specific insights of this work are: (i) significant residual contrast remains after the first pass of a 0.1–0.15 mmol/kg bolus of Gd contrast injected intravenously; (ii) measured in vivo bolus profiles can be approximated by a combination of first pass and residual phase gamma-variate functions; (iii) the analytical PSF expresses the square root dependence of FWHM on TR and Y and Z fields of view; consequently, resolution is maximized when these quantities are reduced as much as possible; and (iv) acquisition times of the order of 45 sec or more are well warranted when scan time is not limited by motion and/or breath-holding. Such is the case for the head and neck where scan times can potentially be 1 min or longer, within the signal-to-noise ratio (SNR) limitations imposed by decreased voxel size.

Although specific model calculations (two-phase gamma-variate) were presented, important aspects of the results are entirely model-independent. For example, the functional dependence of the parameter, M (Eq. (3c)), illustrates that TR and the two FOVs are on equal footing in determining the PSF, regardless of the contrast bolus uptake model. As a consequence, reducing FOV in either phase encoding direction, improves resolution in both of the phase encoding directions. Given this isotropy of the FOV dependence on spatial resolution, the use of an “asymmetric” or “rectangular” FOV to reduce FOV in either phase encoding direction is particularly beneficial with this view order. Further, by adapting the mapping from time to k-space, the analysis presented here can be generalized to other view orders if desired.

The focus of this work is the determination of spatial resolution imposed by the bolus modulation. Although this analysis did not directly address SNR penalties that would result from reduced TR and sparser sampling as a consequence of FOV reduction, this has been considered by others (35–38). It is interesting to note that the peak value of the PSF depends on the inverse of TR and the phase encoding FOVs (Eq. [5]). Consequently, SNR losses predicted for fast TR imaging at reduced FOV will be partially mitigated by the more favorable k-space weightings, assuming scan time is long compared to the contrast bolus modulation. In addition we are fortunate in that the contrast enhancement, b(t), has a prolonged tail as measured in this work. Consequently, high resolution, venous-suppressed, images of the carotid and vertebral arteries can be acquired in a single acquisition with a relatively moderate (0.1–0.15 mmol/kg.) dose of Gd contrast with acquisitions of 40 to 50 sec (28). The model derived here suggests that even longer scan times are warranted (Fig. 4).

The measured curves in this work assume a fast bolus injection protocol (20 cm³ Gadoteridol at 3 cm³/sec). A slower injection protocol could provide more prolonged contrast enhancement, and thus higher spatial resolution. However, we have observed empirically that SNR is visibly reduced in the carotid arteries for cases where the peak amplitude of the bolus is reduced (e.g., patients with reduced cardiac output). Thus it is likely that carotid artery imaging will still demand that the central views be acquired while contrast agent concentration is high (i.e., arterial \( T_1 \leq 50 \) msec). Methods that prolong the contrast enhancement while still providing a period of very short \( T_1 \) (e.g., increased contrast agent relaxivity) may provide both high arterial contrast and improved spatial resolution while maintaining high venous suppression when used in combination with the triggered elliptical centric technique.

CONCLUSIONS
The point spread function (PSF) that describes spatial resolution for CE MRA due to the dynamic contrast bolus has been determined analytically for the elliptical centric view order for arbitrary trigger times. Dependencies on MR acquisition parameters and measured bolus profiles have been shown explicitly. Inherent theoretical limits on spa-
FIG. 5. a: Full coronal MIP of a typical MR angiogram of the carotid and vertebral arteries obtained using the triggered elliptical centric technique with a $20 \text{ cm} \times 15 \text{ cm} \times 6 \text{ cm}$ FOV, a 6.5 msec TR, and a 44 sec scan time. The raw data for this study were zero replaced, reconstructed and displayed as targeted sagittal MIP projections for simulated scan times of 11, 22, 33, and 44 sec, (b–e). The results demonstrate improved spatial resolution and increased signal in the stenosis of the right internal carotid artery (arrowhead) with increasing scan time as predicted by the model. f: Comparison with corresponding X-ray angiogram.
Here we derive an expression for the point spread function (PSF) due to a bolus profile represented by a gamma-variate function having a specific $t^2$ dependence:

$$\hat{b}(t) = (1/2\tau^2) \cdot t^2 \cdot e^{-t/\tau}. \quad [A1]$$

As shown in the text, measured bolus profiles can be represented as the sum of two such functions. In Eq. [A1], $\tau$ is the characteristic time constant, and the factor $1/2\tau^2$ area normalizes $b(t)$. The peak of $b(t)$ occurs when $t = 2\tau$. With a triggered 3D MRA sequence, data acquisition starts at some time $t > 0$. Therefore, to mimic an arbitrary trigger time along $b(t)$, we time shift $b(t)$ by positive fractions, $f$, of the time constant $\tau$.

$$b(t) = \hat{b}(t + f\tau) = e^{-t/f\tau} \cdot e^{-t/2\tau^3 + f \cdot t/\tau^2 + f\tau} \quad [A2]$$

where $b(t)$ is now the bolus profile as measured by the 3D sequence, $t$ is the elapsed time after triggering the 3D acquisition, and $f\tau$ is the trigger time with respect to contrast arrival.

The modulation caused by $b(t)$ is mapped to $k_y-k_z$ space by the specific phase encoding order used. Fourier transformation then provides the PSF. For the specific case of the elliptical centric view order, the $k$-space area accumulated after elapsed time $t$ is a disk centered about the origin. Thus, the specific $k$-space radius, $k$, sampled at a given time $t$ in the acquisition is

$$\int_0^\infty 2\pi k' \cdot dk' = Mt \quad [A3]$$

where $M$ is the time rate of $k$-space area coverage

$$M = \frac{\Delta k_y \cdot \Delta k_z}{TR}, \quad [A4]$$

and $k(t)$ is the radial $k$-space variable

$$k^2(t) = k^2_y(t) + k^2_z(t). \quad [A5]$$

Integrating Eq. [A3] and solving for $t$ using Eq. [A4] gives

$$t = \frac{\pi \cdot TR}{\Delta k_y \cdot \Delta k_z} k^2(t). \quad [A6]$$

Substitution of Eq. [A6] into Eq. [A2], maps the time-shifted bolus profile to $k$-space

$$H(k) = e^{-f} \cdot \left( \frac{\pi^2}{2M^2\tau^3} k^4 e^{-(n/M)k^2} + \frac{f\pi}{M\tau^2} k^2 e^{-(n/M)k^2} + \frac{f^2}{2\tau} e^{-(n/M)k^2} \right). \quad [A7]$$

The PSF, $h(r)$, is obtained by taking the inverse 2D Fourier transform of $H(k)$. The radial symmetry of $H(k)$ of Eq. [A7] permits use of the Hankel transform (29), and the following transform pairs and relationships are known:

$$e^{-mk^2} \Leftrightarrow e^{-\pi r^2} \quad [A8a]$$

$$k^2 e^{-mk^2} \Leftrightarrow \frac{1}{\pi} \cdot \frac{1}{\pi} e^{-\pi r^2} \quad [A8b]$$

$$4\pi^2 k^2 F(k) \Leftrightarrow \frac{d^2 f(r)}{dr^2} + \frac{1}{r} \cdot \frac{df(r)}{dr} \quad [A8c]$$

where in the last equation $F(k)$ and $f(r)$ comprise a Hankel transform pair. By using these relationships we get an expression for $h(r)$, the Hankel transform of $H(k)$:

$$h(r) = e^{-f} e^{-\pi M\tau r^2} \cdot \left[ M(1 + f + \frac{1}{2}f^2) - \pi M^2\tau(2 + f) \cdot r^2 + \frac{1}{2}\pi^2 M^3\tau^2 \cdot r^4 \right]. \quad [A9]$$
The result of Eq. [A9] expresses the PSF resulting from the single gamma variate bolus profile of Eq. [A1], triggered at time $t_f$ after contrast arrival. As shown in the text, the actual model used for the in vivo bolus curves is the sum of an arterial first pass curve, $b_1(t)$, with time constant $t_1$ triggered at peak contrast ($f = 2$ in Eq. [A2]), and a residual curve $b_2(t)$ which is initiated at the peak of the arterial first pass curve ($f = 0$ in Eq. [A2]) and which has a time constant $t_2$:

$$b(t) = b_1(t) + b_2(t) \quad [A10a]$$
$$b(t) = c_1(t^2 + 4t_{\tau_1} + 4\tau_1^2) \cdot e^{-\frac{t}{t_1}} + c_2 \cdot t^2 \cdot e^{-\frac{t}{t_2}} \quad [A10b]$$

where $\tau_1$ and $\tau_2$ and the relative amplitudes $c_1$ and $c_2$ are fitted to the data.

**REFERENCES**