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Flow velocity maps measured by nuclear magnetic resonance in medical intravenous catheter needleless connectors

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ABSTRACT

This work explains the motivation, advantages, and novel approach of using velocity magnetic resonance imaging (MRI) for studying the hydrodynamics in a complicated structural biomedical device such as an intravenous catheter needleless connector (NC). MRI was applied as a non-invasive and non-destructive technique to evaluate the fluid dynamics associated with various internal designs of the NC. Spatial velocity maps of fluid flow at specific locations within these medical devices were acquired. Dynamic MRI is demonstrated as an effective method to quantify flow patterns and fluid dynamic dependence on structural features of NCs. These spatial velocity maps could be used as a basis for groundtruthing computational fluid dynamics (CFD) methods that could impact the design of NCs.

1. Introduction

Mapping fluid flow patterns in a complicated geometry is of interest for diverse biomedical, pharmaceutical and numerous engineering applications. Needleless connectors (NCs) are broadly used medical devices with complicated internal designs [1]. Structural features such as complex surface geometry generate tortuous fluid flow paths and lead to flow complexity that may impact bacterial deposition and biofilm formation [2] and lead to increased risk of blood stream infections in patients [3]. It is useful to visualize in detail the fluid transport and velocity distribution dependence on fluid pathways, dead spaces and stagnation zones in NCs of different designs, to provide data for eventual correlation of these dynamics to issues like bacterial deposition.

NCs, as part of intravenous (IV) therapy and catheter systems, were introduced to medical markets at the beginning of the 1990s. This implementation significantly reduced the risks and complications related to accidental needlestick injuries in health care professionals [4,5]. However, the attachment of pathogenic microorganisms to the inert surface of fluid delivery systems, their constituents and associated living tissues causes formation of bacterial biofilms [3]. Further pathogenic bacterial colonization of medical devices in health care settings leads to an increased risk of infection and clinical treatment failures caused by antibiotic resistance [3,6]. Significant scientific research has investigated how bacterial particle deposition, and subsequent biofilm formation, structure, and development in different flow configurations are influenced by hydrodynamic conditions, surface properties, and channel and flow cell geometry [2,7–13].

The study of fluid flow in complicated geometrical structures requires special methods that are often costly and time-consuming. Computational fluid dynamics (CFD) is widely used to determine flow patterns and give descriptions of the fluid transport in pharmaceutical, medical and engineering systems. However, experimental results are necessary to support and improve the accuracy of CFD experiments. Magnetic resonance imaging (MRI) techniques are now routinely used in the medical field including for the measurement of blood flow [14]. One of the main advantages of MRI is the possibility of quantifying the complexity of fluid flow and hydrodynamic effects in different geometries in a non-invasive and non-destructive way. Magnetic resonance velocity imaging is known as an effective method to measure and provide the details of fluid flow structure [15]. Xia, Callaghan and Jeffrey applied

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this method to visualize flow patterns in sudden contraction and expansion flows and provided accurate spatially resolved velocity measurements [16]. That early experimental work was fundamental in presenting dynamic MRI as an effective tool to reveal secondary flow features in complex geometries. Dynamic MRI measurements have also been applied to directly measure all three velocity components in hydrodynamic instabilities, such as supercritical Taylor number in Couette flow [17], providing details on the internal structure and asymmetry of the vortices.

MRI has a broad spectrum of techniques to examine fluid dynamics and characterize fluid behavior in pharmaceutical and engineering research. Rudin and Sauter in their study [18] implemented MRI and dynamic MRI for drug development studies based on evaluation of a rat model. Manz et al. investigated flow patterns around bacterial clusters [19] obtaining flow velocity maps via dynamic MRI. Zhang and Webb [20] found similarities in the results of CFD and MRI velocity techniques obtaining the velocity fields in flow cells for microseperations. Dynamic MRI has been demonstrated as a non-destructive method for fluid flow studies in biomedical engineering [21,22] and in incorporation of CFD and MRI methods in the study of blood flow [23] as well as many other systems [24].

This research demonstrates that dynamic MRI provides quantitative velocity data for comparison to CFD models which can impact biomedical engineering device design. MRI velocity imaging experiments presented in this work provide a detailed comparison of the three velocity components at numerous spatial positions in six medical NCs of different design. It is shown that the internal device structure has a significant impact on velocity profiles. These experiments validate that MRI velocity measurements are an effective technique to accurately measure the velocity field and characterize transport due to complexity of the geometry in opaque systems such as off the shelf medical devices. The data provide a basis for future studies of the correlation between transport of bacterial pathogens in NCs and the flow field, which could be controlled through design.

2. Theory

2.1. Magnetic resonance imaging velocimetry

Dynamic MRI is an efficient and non-destructive technique to study fluid flow. A velocity imaging pulse sequence or timing diagram of radiofrequency (rf) pulses and magnetic field gradients is shown in Fig. 1 in the supplementary materials. It is the combination of a standard MRI spatially resolved technique with a pulsed gradient spin echo (PGSE) technique that includes the addition of a bipolar gradient pair [15]. The proton ^{1}H, referred to as a spin, is an object of manipulation for the rf pulses and the three orthogonal gradients. Dynamic MRI is based on tracking spin positions in space and encoding for their displacement over an experimentally controlled displacement time.

The application of a magnetic field gradient of amplitude g with duration time δ generates a phase shift of the spin magnetization which defines their initial position. Observation or displacement time $\Delta \gg \delta$ is the time between the first and second gradient pulses. The second pulsed gradient with the same amplitude $\boldsymbol{g}$ and duration time δ unwraps a portion the phase depending on the final position of the spins. The spin displacement from original point $\boldsymbol{r}$ to final point $\boldsymbol{r}'$ generates a net phase shift dependent on the gradient area $\delta\boldsymbol{g}$

$$\phi(\boldsymbol{r}) = \gamma\delta\boldsymbol{g}\cdot\left(\boldsymbol{r}' - \boldsymbol{r}\right) \tag{1}$$

where γ is a gyromagnetic ratio ($\gamma = 2.675 \times 10^8$ rad s^{-1} T^{-1} for the hydrogen proton).

The form of the normalized spin echo signal measured by the top two lines of the experiment in Fig. 1 (supplemental materials) is represented by

$$E(\boldsymbol{g}, \Delta) = \frac{S(\boldsymbol{g}, \Delta)}{S(0, \Delta)} = \iint \rho(\boldsymbol{r}) P_s(\boldsymbol{r}|\boldsymbol{r}', \Delta) \exp(i\gamma\delta\boldsymbol{g}\cdot[\boldsymbol{r}' - \boldsymbol{r}]) d\boldsymbol{r}' d\boldsymbol{r} \tag{2}$$

where $\rho(\boldsymbol{r})$ is the initial spin density, and $P_s(\boldsymbol{r}|\boldsymbol{r}', \Delta)$ is the propagator of the motion, i.e., the conditional probability for a spin to displace to final position $\boldsymbol{r}'$ at time $t = \Delta$ given it was at r at $t = 0$ [25,26]. Introducing the reciprocal displacement wave vector, $\boldsymbol{q} = \frac{\gamma\delta\boldsymbol{g}}{2\pi}$, Eq. (2) can be written

$$E(\boldsymbol{q}, \Delta) = \iint \rho(\boldsymbol{r}) P_s \exp\left(i2\pi\boldsymbol{q}\cdot\left[\boldsymbol{r}' - \boldsymbol{r}\right]\right) d\boldsymbol{r}' d\boldsymbol{r} \tag{3}$$

Defining the average propagator as $\overline{P_s}(\boldsymbol{R}, \Delta) \int \rho(\boldsymbol{r}) P_s(\boldsymbol{r}|\boldsymbol{r}', \Delta) d\boldsymbol{r}$, gives the probability of displacement, $\boldsymbol{R} = \boldsymbol{r}' - \boldsymbol{r}$, during the observation time Δ for all spins averaged over the initial configuration and the MRI signal is defined as

$$E(\boldsymbol{q}, \Delta) = \int \bar{P}_s(\boldsymbol{R}, \Delta) \exp(i2\pi\boldsymbol{q}\cdot\boldsymbol{R}) d\boldsymbol{R} \tag{4}$$

Eq. (4) shows that the average propagator $\overline{P_s}(\boldsymbol{R}, \Delta)$ is the Fourier transform of the measured signal $E(\boldsymbol{q}, \Delta)$with respect to $\boldsymbol{q}$ and is obtained directly from the experiment.

The MRI experiment is based on the excitation of certain nuclei, *i.e.* spins, in the presence of a strong applied magnetic field, B_0 and the application of the linear magnetic field gradient, $\boldsymbol{G}$. The precession frequency of the nuclear spins differs depending on spin location $\boldsymbol{r}$ across the sample and is given by $\omega(\boldsymbol{r}) = \gamma(B_0 + \boldsymbol{G}\cdot\boldsymbol{r})$. The signal obtained from the sample of spin density, $\rho(\boldsymbol{r})$ is a result of the multiplication of an unperturbed NMR signal with a phase factor $\exp(\phi(\boldsymbol{r}))$ where $\phi(\boldsymbol{r}) = \gamma\boldsymbol{G}\cdot\boldsymbol{r}t$ is the phase shift caused by a spread in frequencies due to application of the spatial encoding gradient $\boldsymbol{G}$. Integrating over the entire sample volume, the MRI signal is given by

$$S(t) = \int\int\int \rho(\boldsymbol{r}) \exp[i\gamma\boldsymbol{G}\cdot\boldsymbol{r}t] d\boldsymbol{r} \tag{5}$$

It is again convenient to express this acquired signal in terms of the concept of a reciprocal space vector, $\boldsymbol{k} = \frac{\gamma\boldsymbol{G}t}{2\pi}$ and the signal acquired in $\boldsymbol{k}$-space, can be rewritten in wave vector notation as

$$S(\boldsymbol{k}) = \int\int\int \rho(\boldsymbol{r}) \exp[i2\pi\boldsymbol{k}\cdot\boldsymbol{r}] d\boldsymbol{r}. \tag{6}$$

The Fourier transformation of the NMR signal from Eq. (6) generates the local nuclear spin density function or image

$$\rho(\boldsymbol{r}) = \int\int\int S(\boldsymbol{k}) \exp[-i2\pi\boldsymbol{k}\cdot r] d\boldsymbol{k} \tag{7}$$

Combination of the imaging technique with motion detection, termed dynamic MRI or MRI velocimetry, provides direct, noninvasive, quantitative measurement of the spatial distribution of the velocity field, $\boldsymbol{v}(\boldsymbol{r}) = \boldsymbol{R}/\Delta$.

3. Materials and methods

MRI velocity data were acquired on a Bruker 300 MHz vertical super wide bore magnet networked to a Bruker Avance III spectrometer and equipped with a Micro 2.5 three-dimensional gradient probe (1.48 T/m at 60 A) and a 15 mm diameter ^{1}H radiofrequency (rf) coil. All experiments were conducted at a constant temperature of 20 °C.

Six commercially available NCs from five major manufacturers (Table 1) were used in this study. A single NC was connected to a