Modeling of the optimal scenario of arteriovenous malformation embolization

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Abstract. Cerebral arteriovenous malformation is a congenital developmental pathology of cerebral vessels, in which the arterial and venous blood vessels are connected directly by randomly interlaced degenerate vessels. This is a dangerous disease affecting the functioning of the brain, at which the risk of intracerebral hemorrhage is high. One of the methods of treatment of arteriovenous malformation is embolization – endovascular filling of arteriovenous malformation vessels with a special medical embolizing composition for blocking blood flow through them. This method is widely used, but still in some cases accompanied by intraoperative rupture of arteriovenous malformation. In this paper, on the basis of a one-dimensional model of joint two-phase filtration of blood and an embolizing composition, the optimal scenario of embolization is studied from the point of view of safety and efficiency. The methods of admissible and optimal embolization, which reduce the risk of rupture of arteriovenous malformation vessels, are considered.

1. Introduction
Cerebral arteriovenous malformation (hereinafter referred to as “AVM”) is a congenital pathology of cerebral vessels which is characterized by a direct blood discharge from arterial to venous system, bypassing the capillary network. AVM might cause ischemia of a nearby medulla. In addition, more than half of the patients suffer from hemorrhage (stroke) during their lifetime [1]. Currently, endovascular embolization is the most advanced method of AVM treatment [2]. It basically is the selective blood vessels shutdown by a special embolizing composition (hereinafter referred to as “embolic agent”). Despite the well-developed technique of embolization operations, the risk of intraoperative vascular rupture is still of concern. Baharvahdat et al. in the study [3] noted that 11% of 408 patients with AVM who had got endovascular treatment had hemorrhagic complications associated with treatment. In this regard, AVM embolization modeling is an important task.

2. Model description
Blood and embolic agent movement through racemose small–vascular AVM can be modeled as two-phase filtration process. For simplicity, we assume the homogeneity of the AVM structure and consider one-dimensional case. For this case, a mathematical description was first proposed by S. Buckley and M. Leverett [4]. It is based on the introduction of the concepts of saturation, absolute and relative phase permeabilities [5]. This method, in application to the embolization process, is described in detail in the previous paper [6].
3. Initial-boundary problem
Denote space variable with \( x \), where 0 corresponds to AVM inlet (feeding artery), and \( L \) corresponds to AVM outlet (draining vein). Denote time variable with \( t \), where \( T \) stays for the embolization end time. \( S(x, t) \), \( S \in [0, 1] \), represents blood concentration which initially is identically equal to one. The inlet blood concentration is given by function \( g(t) \), \( t \in (0, T] \). Thus, we get the following initial-boundary problem:

\[
\frac{\partial S}{\partial t} + \frac{\partial b(S)}{\partial x} = 0,
\]

\[
S(0, x) = S_0(x) \equiv 1, \quad x \in [0, L],
\]

\[
S(t, 0) = g(t) \in [0, 1], \quad t \in (0, T],
\]

where \( b(S) \) is the Buckley-Leverett function.

4. Finite-difference scheme
The stated problem is hyperbolic. Thus, its solutions might have discontinuities. Note, that since Buckley-Leverett function is not strictly convex, single increasing and decreasing concentration discontinuous waves, rarefaction waves as well as composite discontinuous-rarefaction waves might occur [7]. The numerical solution of such equations was studied by many authors, e.g. [8, 9].

In this paper, the numerical analysis of AVM embolization initial-boundary problem (1), (2), (3) was carried out using a modification of the CABARET scheme adapted for nonconvex flow functions [10, 11] which took its origin in the works of A.A. Samarskiy and V.M. Goloviznin [12].

5. Embolization success numerical analysis
The calculations were carried out on a rectangular grid with constant steps in time and space. The safety factor of the numerical scheme was chosen equal to \( z = 0.5 \).

The success of embolization is determined by AVM volume filling completeness along with its cross-section closure by embolic agent. The figure 1 shows a good scenario of embolization. The boundary conditions in this case have the following form:

\[
g(t) = \begin{cases} 
0, & 0 < t \leq 2, \\
(t - 2)/10, & 2 < t < 12, \\
1, & 12 \leq t.
\end{cases}
\]

Despite the fact that at first only embolic agent is fed, on the embolization front it occupies only \( \approx \frac{3}{4} \) of the cross-section (which can be seen in figure 1, where at the embolization front the blood saturation is \( S \approx \frac{1}{4} \)). This is due to the decay of the discontinuity formed at the initial moment, which is unstable according to the Oleinik-Liu criterion [7]. Further, with decreasing embolic agent intake, its concentration near the AVM input continues to decrease, but since in this case the posterior discontinuity moves slower than the anterior one, in this scenario the concentration of embolic agent on the anterior discontinuity will not decrease and the AVM section will be cut off by an embolic agent not less than \( \approx \frac{3}{4} \) at all times.

The following example shows a bad scenario of embolization and is presented in figure 2. The boundary conditions are as follows:

\[
g(t) = \begin{cases} 
0, & 0 < t \leq 2, \\
(t - 2)/8, & 2 < t < 10, \\
1, & 10 \leq t.
\end{cases}
\]
Figure 1. A good scenario of embolization. Consecutive stages of the process development at (a) $t_n = 50$, (b) $t_n = 200$, (c) $t_n = 280$. Black dots correspond to a numerical result and the dashed line is its linear interpolation.

Here the beginning of the operation is the same as in the previous example, but the incoming concentration of the embolic agent decreases more rapidly than in the previous case. As a result, the posterior shock wave catches up with the anterior one and cross-section cut off by embolic agent starts to decrease monotonically (figure 2, (c)).

Figure 2. A bad scenario of embolization. Consecutive stages of the process development at (a) $t_n = 80$, (b) $t_n = 130$, (c) $t_n = 230$. Black dots correspond to a numerical result and the dashed line is its linear interpolation.

Thus, the success of the operation depends on the method of embolization – whether the section of the AVM will be blocked by the embolic agent the best possible way, or over time a part of the AVM section previously blocked by the embolic agent will be reopened for blood flow. The AVM cross-section opening for blood flow is characterized by $\min_{x \in [0,L]} S(T,x)$, which will have small values for good scenarios.

6. Embolization degree constraint

We will call the fraction of the AVM vascular space occupied by the embolic agent at a certain point in time as the embolization degree. It can vary from 0% to 100%. In the work [13] it was shown that embolization degree exceeding 60% increases the risk of complications and lethal cases. Thus, we will use this value as an AVM rupture risk characteristic.

7. Optimal embolization problem

Considering the above, the following optimal embolization problem is proposed:

To get maximal AVM filling and cross-section cut off by embolic agent under the following constraints:

(i) Embolization degree should not exceed 60%.
(ii) For medical reasons embolic agent should not reach the vein (exit of the AVM).
(iii) Only active embolization (when the embolic agent enters the AVM) is of interest.
In other words, it is necessary to choose a boundary control \( g(t) \) such that solution of the problem (1)–(3) delivers a minimum to the functional:

\[
J = (1 - \alpha) \frac{1}{L} \int_0^L S(T, x) dx + \alpha \min_{x \in [0, L]} S(T, x), \quad \alpha \in (0, 1),
\]

and satisfies the following conditions:

\[
\frac{1}{L} \int_0^L S(t, x) dx \geq 0.4, \quad t \in [0, T],
\]

\[
S(t, L) = 1, \quad t \in [0, T],
\]

\[
S(t, 0) = g(t) < 1, \quad t \in (0, T).
\]

The problem is considered for a fixed value of parameter \( \alpha \). Further, this problem in the special embolization mode will be considered for specific patients. It turns out that optimal control \( g \) is the same for all \( \alpha \in (0, 1) \).

7.1. Special linear mode of the embolization process

Buckley-Leverett functions were constructed using the previously presented algorithm and clinical data [6]. These functions are shown in figure 3.

Let \( g(t) \) be a piecewise linear function of a special form:

\[
g(t) = \begin{cases} 
0, & 0 < t \leq p_1, \\
\frac{t - p_1}{p_2}, & p_1 < t < p_1 + p_2, \quad p_1 \geq 0, \quad p_2 > 0, \\
1, & p_1 + p_2 \leq t \leq T.
\end{cases}
\]

Figure 3. Functions Buckley-Leverett, built on clinical data. The points are clinical data. Lines are rational approximation.

Then two parameters \( p_1, p_2 \) (in figures \( p_1 \) corresponds to “shift”, \( p_2 \) corresponds to “incline”) can be used to control the embolic agent flow to the AVM input. We will extend the class of admissible controls (10) by function \( g(t) \) with jump discontinuity at \( t = p_1 \) by admitting zero value of \( p_2 \). To find a solution of the optimal embolization problem in the extended class
of functions (10) numerical calculations were carried out for different values of the $p_1$ and $p_2$ parameters.

Without loss of generality the constant $L$ is set to 30. It means that spatial coordinate $x$ varies from 0 to $L = 30$. The terminal time $T$ was chosen in such a way that for each patient for all embolization scenarios of interest the embolic agent reached the vein. Further calculations have no practical meaning.

![Figure 4](image)

**Figure 4.** The parameter plane of the $p_1 - p_2$ for the patient 1. (a) Time step 500, (b) Time step 650, (c) Time step 750, (d) Time step 1000.

As an example for patient 1 the level lines of embolization degree are constructed with dashed lines on the plane of $p_1 - p_2$ parameters (figure 4). Bold black line corresponds to 60% of embolization degree. To the right of this line there is a risk of AVM rupture. The fill color corresponds to AVM cross-section opening for blood flow. Solid red line shows embolization modes for which concentration discontinuities begin to merge. Thus, only scenarios to the right of this line are considered to be good. A violet background appears when the embolic agent reaches the vein. The gray background shows the area where the period of active embolization is completed (the function $g(t) = 1$ for this time).

The area of parameters corresponding to the admissible embolization modes is located to the left of the bold black line, above the border of the gray area and misses the violet zone. Over the time, the range of admissible parameters narrows.

7.2. The optimal embolization scenario

Consider final states of the embolization process on the plane $p_1 - T$. On this plane lines parallel to the coordinate angle bisector are $p_2$ level lines as follows from formula (10). On the bisector the $p_2$ is zero and it does not make sense to consider a part of the plane below it.
Figure 5. The parameter plane of the $p_1 - T$ for (a) patient 1, (b) patient 2, (c) patient 3.

For the patients with presented in figure 3 Buckley-Leverett functions the cross-section opening degree at the end of active embolization is shown by fill color in figure 5. Dashed black lines are level lines of embolization degree. Bold black line corresponds to 60% of embolization degree. To the right of this line there is a risk of AVM rupture. A violet background appears when the embolic agent reaches the vein.

Let us use gradient descent method for functional (6) and some $\alpha \in (0, 1)$. First, the movement from any point of admissible parameters region along the functional antigradients vector field leads to the border of the region $ABCD$ (figure 5, (b)). Secondly, movement along $ABCD$ boundary in the direction of functional decreasing leads to the point $B$ which is located at the intersection of the bisector of the coordinate angle ($p_2 = 0$) and the bold black line. It means that $B$ is the point that delivers the minimum to the functional. It is easy to see that for all patients all of the above conditions are met. These conditions are qualitative and, therefore, will be carried out for the class of Buckley-Leverett functions close to considered.

The found optimal embolization mode is a step function for which the embolic agent input does not exist for $t = 0$, for $t \in (0, T)$ the AVM input is completely blocked by the embolic agent, and at time $t = T$ embolization is completed. The terminal time $T$ corresponds to 60% of embolization degree.
8. Conclusions
To simulate AVM embolization process the Buckley-Leverett problem formulation was proposed. It describes the combined filtration of blood and embolic agent inside the AVM. Numerical calculations were carried out using an improved CABARET scheme. It was suggested that embolization success is determined, firstly, by how full the AVM volume is filled by embolic agent and, secondly, by how well the AVM section is blocked by it. Buckley-Leverett functions were constructed from clinical data to study the optimal embolization problem. Optimal solution was found numerically in a special case of piecewise-linear embolization mode. The set of admissible parameters was identified. Optimal embolization mode reducing the risk of rupture was found for all patients. It was shown that type of optimal embolization strategy does not differ for all considered patients.

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