Drug-eluting beads for tumor treatment by chemoembolization

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Trans-arterial chemoembolization (TACE, Fig. 1) of unresectable liver metastases has shown significant progresses attributable to both advances in chemotherapeutic agents and embolization techniques. Injected drug-eluting beads (DEB) act as drug delivery systems, combining local ischemic necrosis with direct drug effect. In this view, a prolonged delivery is desirable for an increased therapeutic effect.

<table>
<thead>
<tr>
<th>Material</th>
<th>Drug loading [%]</th>
<th>Drug released [%]</th>
<th>t&lt;sub&gt;75%&lt;/sub&gt; [h]</th>
</tr>
</thead>
<tbody>
<tr>
<td>DC bead™ - doxorubicin</td>
<td>98</td>
<td>27 ± 7</td>
<td>2.2</td>
</tr>
<tr>
<td>Hepasphere™ - doxorubicin</td>
<td>100</td>
<td>18 ± 2</td>
<td>2.2</td>
</tr>
<tr>
<td>DC bead™ - irinotecan</td>
<td>93</td>
<td>102 ± 11</td>
<td>1.1</td>
</tr>
<tr>
<td>Hepasphere™ - irinotecan</td>
<td>90</td>
<td>95 ± 9</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Doxorubicin demonstrated high affinity to both type of beads due to its amine group, as compared to irinotecan whose binding was weaker. These data point out an ionic exchange mechanism of drug delivery.

The aim of this project is two-fold:
(i) To evaluate, in collaboration with interventional radiologists, the ability of clinically used embolization microspheres to incorporate and elute novel anticancer drugs for liver chemoembolization.
(ii) To develop novel hydrogel microspheres for enhanced delivery of anticancer drugs.

Among drugs of interest, doxorubicin and irinotecan hold clinical promises for liver cancer treatment. We evaluated two type of poly(vinyl alcohol)-based hydrogel beads, one bearing sulfonate moieties (DCbead™), the other carboxyl groups (Hepasphere™). Figure 2 illustrates the homogeneous doxorubicin fluorescence obtained after drug loading from sulfonated DCbeads™. Both drugs could be loaded in both types of beads, although with different elution profiles as measured by USP4 method (Table). Only part of the initially loaded doxorubicin could be eluted in saline over one week, in a relatively short time – 75% of the released drug was delivered within 2.2 hrs.

Figure 1: Principle of transarterial chemoembolization using hydrogel microspheres (from www.cpmc.org)

Figure 2: Fluorescent image of a 220 μm diameter doxorubicin-loaded bead indicating homogeneous drug loading.

Hydrogel beads may elute cytostatic agents in a drug- and bead-dependent manner. Incorporation of novel anticancer drugs into vectors showing prolonged release properties may pave the way towards more efficient chemoembolization treatments.

**References**

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