Main Problem Being Addressed

The blood–brain barrier (BBB) is a highly selective permeability barrier that separates the circulating blood from the brain extracellular fluid (BECF) in the central nervous system (CNS). In the event of a glioblastoma, the drugs to be administered aren't able to pass through this barrier. This is because blood–brain barrier allows the passage of water, some gases, and lipid-soluble molecules by passive diffusion, as well as the selective transport of molecules such as glucose and amino acids that are crucial to neural function. Our product aims to provide an easy and effective method to open up the blood brain barrier for administration of drugs, yet close once injection is completed so as to avoid infections.

Summary of the proposed invention

Using a laser, an incision will be created in the blood-brain barrier. This incision will then be lined with a 'smart polymer' that is Electroactive Polymer (EAP). Once the incision is lined, a reverse electric current is applied, causing the incision to open up further. Thus, chemotherapy drugs can be introduced in the brain. Once the first dose is completed, the incision is closed by application of a positive current, and later opened at will for later courses.

Current Status

Recently, doctors in Washington University School of Medicine in St.Louis operated on patients with glioblastoma – the most common and aggressive type of brain cancer – underwent minimally invasive laser surgery to treat a recurrence of their tumors."The laser treatment kept the blood-brain barrier open for four to six weeks, providing us with a therapeutic window of opportunity to deliver chemotherapy drugs to the patients," said co-corresponding author Eric C. Leuthardt. This, however carries a risk of infections being carried directly to the brain, and therefore the patient is required to be kept in a sterile environment, preferably in an ICU. Note that this laser technique has less collateral damage than traditional chemotherapy, with less impact to the immune system.

Manufacture and Usage

The polymer ring will be made out of EAPs(Electroactive polymers), similar to artificial muscles. On application of an induced current, there will be attraction forces and the ring will collapse on itself, causing the incision to close. Later, in order to administer a second course of drugs, the incision can be opened again by applying a reverse electric current. The energy for this, can come from an RF Source using an energy harvester(research on these are being proposed at FITT, IIT Delhi). Another proposed way to do this is to use a polymer that can swell/contract in the presence of a solution (something like shape memory polymers as discussed in class).

Comparitive Benefits and Advantages

Image Alt

This approach gives us a lot of flexibility with respect to treatment. The patient need not be restricted to an ICU as the risk of infections is greatly reduced. Also, it carries all the advantages of the laser incision approach that have been tested(for example, less collateral damage to the patient immune system as drugs are restricted to the brain). Also, it is fairly feasible with current technology, save one requirement which is discussed below

Limitations

One limitation that hampers the feasibility of this product is the application of the polymer ring on the incision. It may be prohibitively difficult to stick the ring to the edges of a laser incision. However, with advances in keyhole surgery, this may become easier

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About BBB

The blood–brain barrier (BBB) is a highly selective permeability barrier that separates the circulating blood from the brain extracellular fluid (BECF) in the central nervous system (CNS).

The blood–brain barrier is formed by brain endothelial cells, which are connected by tight junctions with an extremely high electrical resistivity of at least 0.1 Ω·m.

The blood–brain barrier allows the passage of water, some gases, and lipid-soluble molecules by passive diffusion, as well as the selective transport of molecules such as glucose and amino acids that are crucial to neural function.

Endothelial cells restrict the diffusion of microscopic objects (e.g., bacteria) and large or hydrophilic molecules into the cerebrospinal fluid (CSF), while allowing the diffusion of small or hydrophobic molecules (O2, CO2, hormones)

This “barrier” results from the selectivity of the tight junctions between endothelial cells in CNS vessels that restricts the passage of solutes.[6] At the interface between blood and the brain, endothelial cells are stitched together by these tight junctions,

Several areas of the human brain are not on the brain side of the BBB. Some examples of this include the circumventricular organs, the roof of the third and fourth ventricles, capillaries in the pineal gland on the roof of the diencephalon and the pineal gland.

In contrast to suggestions of an immature barrier in young animals, these studies indicate that a sophisticated, selective BBB is operative at birth.

Thus, infections of the brain are very rare. Infections of the brain that do occur are often very serious and difficult to treat. Antibodies are too large to cross the blood–brain barrier, and only certain antibiotics are able to pass.[13] In some cases a drug has to be administered directly into the cerebrospinal fluid (CSF).[14][15] However, drugs delivered directly to the CSF do not effectively penetrate into the brain tissue itself, possibly due to the tortuous nature of the interstitial space in the brain

There are also some biochemical poisons that are made up of large molecules that are too big to pass through the blood–brain barrier

In its neuroprotective role, the blood–brain barrier functions to hinder the delivery of many potentially important diagnostic and therapeutic agents to the brain. Therapeutic molecules and antibodies that might otherwise be effective in diagnosis and therapy do not cross the BBB in adequate amounts.

Mechanisms for drug targeting in the brain involve going either “through” or “behind” the BBB. Modalities for drug delivery/Dosage form through the BBB entail its disruption by osmotic means; biochemically by the use of vasoactive substances such as bradykinin; or even by localized exposure to high-intensity focused ultrasound (HIFU).Mechanisms for drug targeting in the brain involve going either “through” or “behind” the BBB. Modalities for drug delivery/Dosage form through the BBB entail its disruption by osmotic means; biochemically by the use of vasoactive substances such as bradykinin; or even by localized exposure to high-intensity focused ultrasound (HIFU).[21] Other methods used to get through the BBB may entail the use of endogenous transport systems,

Methods for drug delivery behind the BBB include intracerebral implantation (such as with needles) and convection-enhanced distribution

Recently, researchers have been trying to build liposomes loaded with nanoparticles to gain access through the BBB. More research is needed to determine which strategies will be most effective and how they can be improved for patients with brain tumors.

Meningitis is an inflammation of the membranes that surround the brain and spinal cord (these membranes are known as meninges). Meningitis is most commonly caused by infections with various pathogens, examples of which are Streptococcus pneumoniae and Haemophilus influenzae. When the meninges are inflamed, the blood–brain barrier may be disrupted.

A brain or cerebral abscess, like other abscesses, is caused by inflammation and collection of lymphatic cells and infected material originating from a local or remote infection. Brain abscess is a rare, life-threatening condition.

Current Latest

“The laser treatment kept the blood-brain barrier open for four to six weeks, providing us with a therapeutic window of opportunity to deliver chemotherapy drugs to the patients,” “This is crucial because most chemotherapy drugs can’t get past the protective barrier, greatly limiting treatment options for patients with brain tumors.

But the new research marks the first time the laser has been shown to disrupt the blood-brain barrier, which shields the brain from harmful toxins but inadvertently blocks potentially helpful drugs, such as chemotherapy.

Using an incision of only 3 millimeters – about the thickness of two pennies – a neurosurgeon robotically inserts the laser to heat up and kill brain tumor cells at a temperature of about 150 degrees Fahrenheit.

The researchers are planning another clinical trial that combines the laser technology with chemotherapy and immunotherapy as well as trials to test targeted cancer drugs that normally can’t breach the blood-brain barrier.

Idea

A ring of smart materials like as shown in class : they shrink in the presence of a certain electrical impulse. So, we will perform a laser incision as before, but line the hole with such a smart polymer. When drugs are to be administered, we apply a reverse voltage and the ring opens up. Once they are administered, apply a positive current - the hole is now closed.
This reduces the chance of infection over the 4–5 weeks that the therapy continues.