NAPS (Nano Artertract Plaque Seeker)

Abstract

Coronary artery disease (CAD) is a partially hereditary disease that affects over 20 million adults in the United States, killing over 350,000 people per year. People with CAD often have high levels of plaque buildup in their arteries, which narrows the arteries and reduces blood flow to vital organs. This can lead to recurring heart attacks and even heart failure. However, with our new technology, the NAPS (Nano Artertract Plaque Seeker), we can reduce plaque buildup and prevent patients from having further heart complications. NAPS is a drug, released via an intravenous injection, that targets plaque-causing macrophages. Iron oxide nanoparticles in the drug will aid with precise localization of drug delivery through a magnetic field, which will be provided by hospitals utilizing this technology. This treatment is a more efficient and precise approach to combat heart disease. With NAPS, there will no longer be any unprecedented "NAPS"!

Present Technology

The treatment of coronary artery disease (CAD) involves a combination of medications, lifestyle changes, and medical procedures. While these treatments are effective to different degrees, they each come with limitations that highlight the need for more advanced solutions like NAPS.

Medications play a key role in managing CAD by addressing risk factors and preventing complications. Statins work by inhibiting an enzyme in the liver responsible for cholesterol production, thereby lowering LDL levels. However, they can cause side effects such as liver damage and muscle pain. Anticoagulants and antiplatelet drugs prevent blood clots, reducing the risk of heart attacks and strokes, but they increase the risk of bleeding. While these medications are effective in managing symptoms, they do not directly address the root cause of plaque buildup. NAPS, on the other hand, targets plaque-causing macrophages directly, offering a more precise and effective approach to treating CAD.

Minimally invasive procedures, such as angioplasty and stent placement, are commonly used to treat narrowed or blocked arteries. During angioplasty, a balloon is inflated to widen the artery, and a stent may be placed to keep it open. While these procedures are less invasive than surgery, they carry risks such as restenosis (re-narrowing of the artery) and infection. Additionally, they do not address the underlying plaque buildup and may require repeat procedures. NAPS offers a non-invasive alternative by using targeted drug delivery to reduce plaque and stabilize arteries, eliminating the need for repeated interventions.

For severe cases of CAD, coronary artery bypass grafting (CABG) is often the last resort. This surgical procedure involves creating new pathways for blood flow by grafting veins or arteries from other parts of the body to bypass blocked coronary arteries. While CABG can

significantly improve blood flow, it is highly invasive, requiring a large incision in the chest and a lengthy recovery period. Risks include infection, complications from surgery, and long-term graft failure. NAPS, with its non-invasive approach and targeted treatment, could provide a safer and more effective alternative for patients with advanced CAD.

Current diagnostic technologies, such as intravascular ultrasound (IVUS) and near-infrared spectroscopy (NIRS), allow doctors to visualize plaque and assess blood flow dynamics. These imaging techniques rely on sound waves or light to provide detailed information about plaque composition and artery health. However, they are limited to diagnosis and cannot actively treat plaque buildup. NAPS integrates imaging capabilities with targeted therapy, allowing for real-time monitoring and treatment of plaque, bridging the gap between diagnosis and intervention.

Despite the advancements in current treatments, significant limitations remain. Medications manage symptoms but do not eliminate plaque, while invasive procedures carry risks and require recovery time. Diagnostic technologies provide important insights but lack therapeutic capabilities. NAPS addresses these gaps by combining precise drug delivery, magnetic targeting, and real-time imaging into a single, non-invasive treatment. By targeting the root cause of plaque buildup and offering a safer, more effective solution, NAPS has the potential to revolutionize the treatment of CAD.

History

Studies showed that plaque buildup in the arteries, a main cause of Coronary Artery Disease (CAD), has been prevalent since ancient Egyptian times. Discovered in 2009 by the American Heart Association, Egyptian mummies like Pharaoh Merentaph, who died 1203 BCE, were found to have clogged arteries, now known as Atherosclerosis. Another early discovery of CAD was made by Leonardo Da Vinci around 1506. After conducting an autopsy on a deceased

man in Florence, Da Vinci noticed the narrowed state of blood vessels near bifurcations, where the arteries branch off into two. A few decades later in the 17th century, significant medical discoveries around the heart emerged. William Harvey, a physician to English monarchs, discovered that blood circulation revolved around the heart in a circular motion. Followed by Freidrich Hoffmann, a professor of medicine at Halle University published his novel, *Medicina Rationalis Systematica*, which further revealed the nature of heart disease and was the first to emphasize the narrowing of the heart's arteries which to this day is known as Coronary Artery Disease.

The earliest type of treatments for CAD were not seen until the 1960's and 1970's with the bypass surgery and balloon angioplasty procedures. Coronary Artery Bypass Graft (CABG), also called heart bypass surgery, is often the last resort since life expectancy after CABG is only about 18 years. Alternatives to this surgery are angioplasty procedures. During this procedure, a catheter is inserted into your blood vessel and guided to the location of your blocked artery. There, a little balloon is inflated to remove plaque and widen the artery. The 1980's came with the use of stents made from meshed coils used to push open arteries narrowed by plaque buildup.

The use of nanoparticles in medical treatments dates back to the early 2000s when researchers began exploring its potential for targeted drug delivery. Initially, nanoparticles were used for cancer treatment, as their small size allowed for the precise targeting of tumors. Over time, technology evolved and scientists started investigating its applications in cardiovascular diseases. The concept of using magnetic fields to guide nanoparticles emerged from research in magnetic resonance imaging (MRI), where magnetic nanoparticles were used as contrast agents to enhance imaging quality.

Future Technology

In 10 or more years, NAPS (Nano Artertract Plaque Seeker) will revolutionize the treatment of coronary artery disease (CAD) by providing a non-invasive, highly targeted approach to eliminating arterial plaque. With the NAPS treatment, patients are administered an intravenous injection of the drug, which contains iron oxide nanoparticles, that can be guided by an external magnetic field to deliver therapeutic agents directly to plaque-causing macrophages. Real-time imaging capabilities allow doctors to monitor the treatment's progress, ensuring optimal results. This ideal integration of therapy and diagnostics will transform CAD treatment, offering a faster, safer, and more effective solution than ever before.

NAPS is a cutting-edge drug delivery system composed of two key components, the drug and the technology. The drug is composed of iron oxide particles, rapamycin, necrostatin-1, cholesterol-lowering-enzymes, and a biocompatible polymer. The technology includes the pulsed electromagnetic field (PEMF), quantum dots, and intravascular ultrasound (IVUS).

Let’s talk about the components that make up the drug. Iron oxide nanoparticles are chosen for their magnetic properties, which allow them to be guided by external magnetic fields to ensure the precise delivery to plaque sites. Additionally, iron oxide is biocompatible and has been extensively researched for medical applications, including cancer treatment and MRI contrast agents. Its safety and effectiveness in the human body make it an ideal choice for NAPS.Rapamycin is ahis drug that promotes macrophage autophagy, a process that reduces inflammation and stabilizes vulnerable plaques by breaking down damaged cellular components.

Necrostatin-1 is an inhibitor that prevents necroptosis and apoptosis in macrophages, This reduces plaque progression by preventing cell death that contributes to plaque instability.

Cholesterol-lowering enzymes, like cholesteryl ester hydrolase, break down cholesterol deposits within plaques, further reducing plaque size and improving arterial health.These drug components will be encapsulated with a biocompatible polymer, such as polyethylene glycol (PEG) or chitosan, to prevent immune system recognition and ensure stability in the bloodstream. These coatings are designed to minimize immune responses and toxicity, making the nanoparticles safe for long-term use.

As for the technology, NAPS uses an external pulsed electromagnetic field (PEMF) to guide the iron oxide nanoparticles to the plaque sites. The PEMF will operate at a frequency of 75-100 Hz, with each exposure lasting 30 minutes. The total exposure time is 60 minutes, with intervals between exposures to prevent thermal effects and ensure patient safety. The magnetic field ensures that the nanoparticles accumulate precisely where they are needed, minimizing off-target effects and maximizing the treatment's effectiveness. In addition, quantum dots and intravascular ultrasound (IVUS) are used for real-time imaging. Quantum dots are fluorescent nanoparticles that allow doctors to track the nanoparticles' movement and drug release in real-time. IVUS provides detailed images of arterial walls, enabling precise monitoring of plaque reduction and treatment efficacy.

NAPS (Nano Artertract Plaque Seeker) represents a significant leap forward in the treatment of coronary artery disease (CAD), offering numerous advantages over existing methods. Unlike invasive procedures such as bypass surgery or angioplasty, NAPS is non-invasive, requiring no incisions or surgical interventions, which drastically reduces recovery time and eliminates the risks associated with surgery, such as infection or complications. The precision of NAPS is uinque, as its magnetic targeting system ensures that therapeutic agents are delivered directly to plaque sites, minimizing damage to healthy tissues and maximizing treatment

effectiveness. Additionally, NAPS is a comprehensive solution, combining therapy and diagnostics into a single treatment, eliminating the need for separate procedures and streamlining the patient experience. By specifically targeting macrophages and reducing inflammation, NAPS addresses the root cause of plaque buildup, offering long-term benefits that extend beyond symptom management. Furthermore, the non-invasive nature of NAPS makes it accessible to a wider range of patients, including those who may not be candidates for surgery due to age, health conditions, or other factors. This combination of safety, precision, and efficacy positions NAPS as a transformative solution for CAD, providing patients with a faster, safer, and more effective treatment option.

We hope for NAPS to be the standard treatment for CAD, available in hospitals worldwide. Patients will receive quick, effective treatment without the risks and recovery time associated with surgery, and medical professionals will use advanced imaging to monitor progress and adjust treatments in real-time. With NAPS, we envision a world where heart disease is no longer a leading cause of death, and patients can live longer, healthier lives.

Breakthroughs

Several breakthroughs are necessary to make NAPS (Nano Artertract Plaque Seeker) a reality. First, the development of biocompatible coatings for the nanoparticles is essential to prevent immune system recognition and ensure stability in the bloodstream. These coatings must be carefully designed to avoid triggering an immune response while maintaining the nanoparticles' ability to deliver drugs effectively. Second, the creation of advanced magnetic guidance systems is required to generate external magnetic fields strong enough to guide nanoparticles without harming surrounding tissues. This involves optimizing the strength and precision of the magnetic fields to ensure accurate delivery of the nanoparticles to the plaque site.

Third, identifying and optimizing therapeutic payloads is crucial for the success of NAPS. Researchers must determine which drugs are most effective at reducing plaque, such as rapamycin for promoting macrophage autophagy and necrostatin-1 for inhibiting necroptosis and apoptosis in macrophages. Additionally, they must develop methods to encapsulate and release these drugs at the target site in a controlled manner, ensuring that the therapeutic agents are delivered precisely where they are needed. This includes optimizing drug-loading capacity, release kinetics, and stability to maximize treatment efficacy while minimizing side effects.

While the individual components of NAPS—such as magnetic nanoparticles, biocompatible coatings, and therapeutic agents—have been researched separately, integrating them into a single, cohesive system presents significant challenges. The precise control required for magnetic targeting, the development of biocompatible coatings that are both effective and safe, and the optimization of therapeutic payloads for plaque reduction are complex tasks that require interdisciplinary collaboration and advanced engineering. Additionally, the long-term effects of nanoparticles in the human body and the scalability of magnetic guidance systems are still areas of active research. These challenges, combined with the need for rigorous testing and regulatory approval, have delayed the realization of technologies like NAPS.

Let’s focus on the therapeutic payload optimization breakthrough, which is critical for ensuring that NAPS delivers the right drugs to the right place at the right time. To evaluate the efficacy of the therapeutic payload, a research project would involve using animal models, such as mice or rabbits with induced atherosclerosis. First, researchers would administer the nanoparticles loaded with drugs like rapamycin and necrostatin-1 intravenously and use imaging techniques like MRI to track their distribution and accumulation in plaque sites. Second, drug release kinetics would be analyzed by monitoring the rate and extent of drug release at the target site through

blood samples and tissue analysis. Third, plaque reduction would be quantified using imaging methods such as MRI or intravascular ultrasound, as well as histological analysis of arterial tissues to assess changes in plaque size and inflammation. Finally, safety metrics would be monitored by analyzing blood work and organ function to detect any adverse effects, such as immune responses or toxicity. This comprehensive data collection would provide critical insights into the efficacy and safety of the therapeutic payload, guiding further development and optimization of NAPS.

Design Process

There were several ideas we had considered previous to the design of NAPS, all which shared a common objective, reducing plaque buildup and therefore treating coronary artery disease (CAD). While some of these ideas seemed compelling, NAPS was chosen because of its practicality, efficacy and efficiency.

Our team considered using magnetic fields to internally heat the nanoparticles and melt away fatty plaque deposits, or using the nanoparticles to improve the accumulation of drugs in plaque areas. While the idea of heating nanoparticles to melt plaque was interesting, it posed risks such as tissue damage from excessive heat and limited effectiveness in targeting deep-seated plaque. Moreover, the technology for precise temperature control in the body is not yet advanced enough for safe implementation. Our team recognized that magnetic fields tend to lose effectiveness over distance which is why the second approach, used in NAPS, is more feasible. Accumulating the drugs in the affected area is more safer and practical compared to the first approach as it has less risks and can stabilize the plaques in the arteries, reducing adverse inflammation.

Another idea our team explored was plaque prevention using high-density lipoproteins (HDLs). HDLs are known to help remove fatty deposits from the bloodstream, which can reduce plaque buildup. Our team considered using medications like niacin, gemfibrozil, simvastatin, or rosuvastatin to increase HDL levels and transport excess fatty material to the liver for disposal. While this approach had potential, it was rejected because HDL-based therapies focus on preventing plaque formation rather than treating existing plaque. Rapmycin and necrostatin-1, on the other hand, help reduce plaque buildup and stabilize vulnerable plaques by promoting macrophage autophagy, which is a process in which cells break down and recycle old or damaged parts of themselves. They can not only quickly get into the blood but were also tested to reduce plaque instability. Since NAPS aims to address advanced CAD, this approach was deemed sufficient for the project's goals than the former. Furthermore, clinical trials for HDL-raising drugs have shown limited success in reducing heart attacks, making the previous option less viable.

The final idea we rejected relates to the delivery method of the drugs. We considered an invasive close-to-the-heart procedure to ensure precise drug delivery, however, due to its various risks, we rejected this idea for one that is not as invasive and more accessible. The risks of such procedures include bleeding, infections, and damage to heart tissue, among other serious complications. An intravenous injection seemed more viable and less intimidating for patients compared to surgical procedures, providing a more comprehensive treatment approach.

Consequences

NAPS has the potential to bring significant positive consequences, such as reducing frequent heart attacks, improving the quality of life for coronary artery disease (CAD) patients,

and lowering healthcare costs associated with invasive procedures. By providing a non-invasive and highly targeted treatment option, NAPS could eliminate the need for many of the risky and expensive procedures currently used to manage CAD. Instead of targeting a general area, NAPS will be able to eliminate specific problem areas where plaque buildup critically needs to be removed. Although NAPS is an innovative approach that has the potential to revolutionize the management of coronary artery disease, it's also important to recognize its potential drawbacks and consequences.

NAPS's nanomagnetic particles can be filtered through the kidney and removed via urine. However, there are potential health risks associated with the long-term use of nanoparticles in the body, such as toxicity and immune reactions. The long-term effects of nanoparticles in the body are not fully understood and require further research to ensure patient safety.

Financially, the large-scale implementation of magnetic field technology may require significant investment and infrastructure development. Another financial concern is the high cost of nanotechnology, an estimation of about $21 million , which could limit access for low-income patients and may worsen healthcare inequality. Producing and disposing of nanoparticles could cause future financial and environmental concerns if not managed and regulated properly.

By addressing these concerns through rigorous safety testing, equitable pricing, and environmentally sustainable manufacturing practices, the benefits of NAPS can be maximized while minimizing potential drawbacks.

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