Advancement on Digestive Tract Biomedical Stents, A Review

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Abstract

Biomedical stents for the digestive tract address many of the limitations associated with traditional surgical treatments for gastrointestinal diseases. This paper provides a review of the performance requirements, complications, and limitations of stent materials in the treatment of common digestive tract diseases. The advantages and disadvantages of different materials and processing technologies for digestive tract stents are discussed. Furthermore, considering the diverse requirements for ideal alimentary canal stent materials, the challenges that require further research are outlined in detail, providing strategic references for the development of biomedical stents for the digestive tract.

Keywords: Biomedical Stents; Digestive Tract; Biodegradable; Functionalization

1 Introduction

Esophageal cancer, gastric cancer, bowel cancer, liver cancer, and other cancers, as well as post-operative stenosis, gastrointestinal obstruction, stones, chronic inflammation, and other diseases, can severely impact both the physiological and psychological well-being of patients, greatly reducing their quality of life. Stents have emerged as an effective treatment option for these conditions, and the choice of stent materials significantly influences patients’ experience [1]. An ideal digestive stent should possess the following characteristics: (1) good biocompatibility to minimize the risk of rejection; (2) adequate plasticity and flexibility for easy placement at the site of lesion; (3) easy expandability, sufficient support strength, and excellent geometric stability and mechanical durability.

This paper provides an overview of digestive tract stents in the context of digestive tract diseases, treatment methods, and clinical needs, as well as material combinations and new engineering innovations. The performance requirements, complications, and future development trends of stent-assisted therapy are discussed. Additionally, the advantages and disadvantages

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of various materials and processing technologies used in stents are reviewed, aiming to promote improved applications of digestive tract stents in the treatment of digestive tract diseases in the future.

# 2 Digestive Tract Stents

## 2.1 Esophageal Stents

Lesions such as esophageal cancer, anastomotic stricture after esophageal surgery, stenosis after chemical corrosive burns, and congenital esophageal stenosis can severely impair esophageal peristaltic function and reduce patient survival rates. Currently, in addition to fully covered esophageal stents, radioactive particle stents and drug-eluting esophageal stents can also be placed to treat dysphagia, addressing both feeding challenges and local tumor treatment. These research-stage stents can be categorized into non-degradable and degradable stents, both of which are pre-fabricated. In addition to conventional stents, tissue engineering is emerging as a new solution to such problems, with the ability to inject material into the affected area to fill various defect shapes and sizes more easily [2].

Nickel-titanium alloy stents [3] are the most commonly used metal stents in clinical practice. They offer good morphological memory function, flexibility, and biocompatibility compared to traditional stainless-steel stents. However, stent placement can also result in complications such as chest pain, bleeding, perforation, stent migration, and restenosis.

Biodegradable materials are a class of polymeric materials that include naturally degradable polymers, microbially synthesized polymers, and synthetic degradable polymers. The degradation principle of biodegradable materials is based on the presence of groups that are unstable to water, such as ester bonds, which can be broken by water molecules in a physiological environment. Natural degradable polymers, such as chitin and chitosan, have better biocompatibility but poor mechanical properties, solubility in water or weak acids and bases, and faster degradation after cross-linking. Currently, synthetic degradable polymers, such as poly(lactic acid) (PLA), poly(propylene glycol) (PGA), polycaprolactone (PCL), poly(p-dioxanone) (PPDO), and poly(levulinic acid) (PLLA), are commonly used, as they offer more flexibility in designing molecular structures to achieve desired material properties through copolymers and blends. The morphology of the biodegradable stent also plays an important role in its therapeutic effect.

3D printing and decellularized tissue engineering are emerging solutions for esophageal conditions, and animal experiments have shown that these new technologies offer improved biocompatibility and therapeutic effects, addressing common challenges faced in the past. The exploration of these new technological fields has become a major direction and focus for researchers in recent years. Decellularized tissue scaffolds are used to reduce the immunogenicity of organs or tissues by removing cellular components while preserving the mechanical and bioactive properties of the organ [4]. One study utilized aminolytic glutaraldehyde cross-linking to graft filamentous proteins onto the scaffold surface, enhancing the hydrophilicity and biocompatibility of the substrate [5].

## 2.2 Gastric Stents

Gastric cancer is the fifth most common malignancy worldwide, with approximately 1 million
new cases diagnosed annually. It is also the third leading cause of cancer-related deaths, with over 720,000 deaths reported each year. The treatment of gastric cancer depends on the stage of the disease, and surgical resection, particularly for early stage gastric cancer (stage II), can result in a cure. Laparoscopic-assisted distal gastrectomy is the most common surgical procedure used for treating gastric cancer. Gastric stenting is a conservative treatment option for patients with intermediate to advanced gastric cancer, esophageal cancer, or other conditions that make eating difficult. For patients who are unable to undergo surgery due to eating difficulties, weakness, or old age, a stent can be placed in the stomach to allow normal eating and resume a normal life.

Singla et al. [6] successfully fixed a self-expanding metal stent (SEMS) to the gastric wall using a multi-loop nylon wire and a viewing clip, a technique that prevents migration of SEMS. Metal materials have significant advantages in terms of fatigue and machinability, making them widely used in stent preparation. Specifically, metallic titanium (Ti) and its alloys have high specificity, high elastic modulus, and excellent biocompatibility, which are beneficial for cell adhesion, proliferation, and differentiation. However, the issue of SEMS stent migration still needs to be addressed.

Due to the non-degradable nature of metal stents, their long-term presence in the human body may cause complications such as inward tumor growth and migration of the stent into the stomach. Biodegradable materials, such as Polycaprolactone, Poly(l-lactic acid) (PLLA), and Poly-Glycolic acid (PGA), have good biocompatibility and mechanical properties, and can be degraded into harmless substances in a mild intra-biological environment. Therefore, they are widely used in biomedical fields. The advantages of biodegradable materials for gastric stents include their ability to be absorbed by the body without causing obstacles to future treatment or forming a potential risk of infection, as well as their gradual softening properties. With the continuous development of processing technologies and materials, it is anticipated that biodegradable stents will be more widely used in gastric stents. However, currently, metal-based stents are more commonly used in clinical applications compared to biodegradable stents. Biodegradable stents may also have some limitations, such as tissue incompatibility with the human body, large thickness of stent beam, slower degradation than expected, insufficient mechanical strength, with only half the strength of metal stents, and inadequate support. Additionally, biodegradable stents may be prone to fracture, stent exposure, and inflammation during the degradation process.

The preparation of stents from biodegradable materials has great potential, as they can be gradually replaced by human cells and can carry bioactive substances for increased therapeutic effectiveness. Meanwhile, many researchers are focusing on 3D printing biodegradable stents that can be produced in specific sizes for individual patients. In conclusion, despite some limitations, the benefits of biodegradable stents generally outweigh the disadvantages, and the therapeutic application of biodegradable gastric stents is a growing trend. In the future, it may be possible to combine different drug-carrying materials to design reservoirs that can accommodate large doses of drugs and improve drug delivery design [7].

2.3 Intestinal Stents

When the abdomen is narrowed or obstructed due to advanced malignant tumors or other malignant lesions, it can cause difficulties in digestion, absorption of food, and defecation. Globally, there are approximately 850,000 new cases of colorectal malignancies each year, with 7% to 29%
of them presenting with acute complete or incomplete bowel obstruction as their first symptom. Bowel preparation before surgery is challenging in cases of colorectal cancer with obstruction, making clinical management more difficult, and increasing the risk of postoperative complications such as anastomotic leak and serious infection, which are fundamental problems in the surgical management of colorectal cancer obstruction.

In recent years, there has been a growing number of reports on the use of various metal stents as intestinal support for the treatment of malignant colorectal obstruction both domestically and internationally. A mesh stent is placed at the site of intestinal stenosis to hold the intestine open, allowing for the reopening of the stenosis or obstruction site. This technique can be used as a permanent or temporary treatment for malignant obstruction in colorectal cancer, creating conditions for elective surgery. Intestinal stents are suitable for patients with stenotic obstruction of the duodenum, small intestine, colon, rectum, and anastomotic stricture due to invasion, compression, or other malignant lesions of advanced abdominal tumors [8]. The use of intestinal stents in the treatment of colorectal cancer obstruction is mainly divided into temporary transitional placement and palliative treatment [9].

Metal stents, such as self-expanding metal stents, have been increasingly used as intestinal stents for the treatment of malignant large bowel obstruction [10, 11]. Metals, such as nickel-titanium memory alloys and stainless steel, are the main material choices for self-expanding colorectal stents [12, 13]. However, metal stents have potential risks, including the potential to affect MRI results, cause perforation of the bowel lining, excessive stiffness, bleeding, perforation, and fistula formation [14-16].

Biocompatible polymer stents can overcome the limitations of metal stents in terms of biodegradability, but they must possess adequate mechanical properties and structural support [17-19]. Silk-based biomaterials have been widely used in clinical settings [20]. Xie et al. developed a drug-coated stent using a silk fibroin (SF) solution mixed with curcumin and 5-fluorouracil, which was then coated onto a degradable intestinal stent using electrospinning. Results showed that the SF drug coating provided sustained drug release for over 400 hours, and its ability to inhibit tumor tissue growth was demonstrated in a murine model [19-22]. Drug-loaded stents have promising potential for the treatment of intestinal cancers in the future [21, 23-25]. Wang et al. validated the in vivo biocompatibility of MAO/PLLA/paclitaxel/Mg-Zn-Y-Nd alloy stents treated with a microarc oxidation process (MAO) surface using a rabbit model. The results showed that the stent effectively inhibited intestinal tissue restenosis and inflammation, and the biocompatibility and biodegradation properties indicated that the degraded waste could be self-metabolized and discharged in vitro [26]. Lin et al. designed a new iron-based drug-eluting stent with a zinc barrier layer, and the rabbit model demonstrated that this stent significantly shortened the corrosion period while maintaining performance, and the metabolites did not cause any biological problems [27]. Therefore, continuously improved biodegradable metals not only maintain their excellent mechanical properties, but also exhibit better compatibility with practical use in terms of biocompatibility and biodegradability. Roldán et al. investigated the use of biodegradable polydioxane stents in the treatment of postoperative colorectal strictures and fistulas, and the results suggested that treatment with biodegradable stents is an effective short-term alternative with minimal complications for colonic strictures and rectal skin fistulas [28]. Photodynamic therapy (PDT) is a novel therapeutic approach [29]. PDT-stent, after light exposure, successfully generated cytotoxic singlet oxygen in the surrounding tissues, inducing apoptotic degradation of tumor cells and regression of xenograft tumors in mouse models. Bi et al. and Wang et al. assisted in the treatment of tumorigenic obstruction by incorporating radioactive particles, such
as $^{125}\text{I}$, $^{188}\text{Re}$, $^{32}\text{P}$, and $^{103}\text{Pd}$ [30, 31]. Tanaka et al. used a new degradable polylactic acid mono-threaded stent for two patients with benign gastroduodenal stenosis, and no complications occurred during placement, with no recurrence of stenosis during the 6-month follow-up period, indicating the effectiveness of the new degradable stent for the treatment of benign gastric and duodenal strictures [32]. These materials may represent the future trend in stent development for the treatment of benign gastric and duodenal strictures.

Fig. 1: (A) 2D images (Micro-CT) of a new iron-based drug-eluting stent with a zinc barrier layer implanted in rabbits at 3 days, 3 months, 6 months, and 13 months [27]; (B) MAO/PLLA/paclitaxel/Mg-Zn-Y-Nd alloy stent [26]; (C) Photograph of a radioactive bare metal stent loaded with $^{125}\text{I}$ particles [31]; (D) Nolydioxide stent (arrows indicate impermeable markers) [28]; (E) Bare metal stent and photodynamic therapy stent with embedded photosensitizer [29]

2.4 Biliary Stents

The biliary tract is responsible for transporting bile from the liver to the duodenum and comprises intrahepatic and extrahepatic bile ducts [33]. Common conditions affecting the biliary tract include biliary strictures, bile duct stones, and biliary obstruction. Interventional biliary stenting is an effective treatment option for these conditions [34].

Devière et al. [35] treated 177 patients with benign biliary stenosis using fully-covered self-expanding metal stents (FCSEMS). The duration of stent retention was 10-12 months for patients with biliary stenosis due to chronic pancreatitis or post-cholecystectomy, and 4-6 months for patients with anastomotic stenosis after liver transplantation. Stent retention duration was longer in all cases, and the overall elimination rate of benign stenosis was 76.3%, with the highest elimination rate observed in cases of benign biliary stenosis due to pancreatitis at 79.7%. However, the elimination rate of stenosis after liver transplantation was 68.3%, which was lower than the elimination rate of stenosis with multiple plastic stents (80%-90%). All stents could be removed endoscopically in the study, and FCSEMS placement significantly reduced the number of endoscopic retrograde cholangiopancreatography (ERCP) procedures.

Patrick et al. [36] used a new intraductal FCSEMS called Niti-S biliary stent, which is made of nickel-titanium alloy wire covered with PTFE. The diameter of the middle part of the stent is 2
mm narrower than both ends, and the diameter at both ends is 8, 10, or 12 mm, with the length ranging from 40 to 80 mm. The distal end of the stent has a 10 cm removable wire that facilitates stent removal in the new catheter. This new stent is more suitable for the treatment of biliary anastomotic stenosis after in situ liver transplantation compared to the conventional fully-covered self-expanding metal stent, and it reduces the displacement rate of the fully-covered metal stent. Non-degradable polymer biliary stents may have anchoring flaps to prevent stent migration, and multiple stents (MPS) can be inserted during each ERCP [37]. However, the main drawback of non-degradable polymer biliary stents is poor stent patency, with obstruction within the stent. The low patency rate is partly due to the formation of bacterial biofilm, bile sludge formation, and bile acid salt deposition leading to stone formation.

To overcome some of the drawbacks associated with non-degradable stents, such as the need for secondary surgery for removal, the use of degradable polymers is clearly advantageous [38]. Among the metals studied for resorbable medical implants, including stents, magnesium (Mg), iron, zinc, and their alloys have shown promise. In recent years, Mg alloys have gained significant interest as absorbable orthopedic fixation devices and coronary stents, with some products already commercialized, such as DREAMS 1G and DREAMS 2G. In Figure 2, Zhang et al. [39] used ZX20 alloy monofilament to prepare a series of biodegradable Mg biliary stents with a diamond-shaped mesh structure, varying monofilament diameters, woven stitch counts, and surface treatments. The effect of the Mg stent structure on the support capacity was evaluated through compression tests.

In summary, interventional implantation of biliary stents is an effective treatment for refractory and complex biliary patients, but its practical clinical application is constrained by the complex environment of the biliary tract. With continued research on biliary stent materials, we can

![Diagram of Mg biliary stent preparation process.](image-url)
further elucidate the mechanism of material-bile interaction in the biliary environment, evaluate the material compatibility index, develop new biliary stent materials, optimize stent structure design to improve mechanical properties, and modify stent surface to alter the interaction between the material and the bile contact interface. These advancements are expected to result in breakthrough developments in biliary stents with fewer complications, longer patency duration, and superior performance.

2.5 Liver Stent Materials

As an essential organ in the human body, the liver plays a critical role in bile secretion, detoxification, protein synthesis, and glycogen storage. However, it is highly susceptible to pathological conditions, and liver diseases such as liver cancer and acute liver failure affect a significant proportion of the population. Globally, viral hepatitis, hepatocellular carcinoma, and complications of cirrhosis are responsible for approximately 2 million deaths each year [40]. Currently, liver transplantation is the main medical treatment for liver diseases, serving as a bridge between liver failure and transplantation. Therefore, the selection of suitable liver scaffolds for preparation is a fundamental research task in liver transplantation. Research on liver tissue engineering scaffold materials is still in the stage of screening for applicability, with the main focus on degradable polymeric materials and natural matrix materials that show promising performance in structural tissue engineering, as listed and compared in Table 1 [11].

Table 1: Comparison of materials, manufacture technologies and features of digestive tract stents [11]

<table>
<thead>
<tr>
<th>Materials</th>
<th>Manufacture technologies and Structures</th>
<th>Features</th>
<th>Refs</th>
</tr>
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<tbody>
<tr>
<td>Nitinol and other metal stents</td>
<td>Braiding; single or double layer braided structure of bare or PU, PTFE and other material coated stents</td>
<td>Surface of stent can be function-alized by coating for drug elution; non-biodegradable; potential risk of causing perforation of the bowel lining</td>
<td>[6, 12, 13, 36]</td>
</tr>
<tr>
<td>Mg-Zn-Y-Nd alloy</td>
<td>Extrusion molding after hot processing; biodegradable metal stent body, bare or outer polymer such as PLLA coated stent</td>
<td>Corrosion resistance; drug-eluting targeted therapy; biodegradability; biocompatibility</td>
<td>[26]</td>
</tr>
<tr>
<td>PDO; PLA; PCL</td>
<td>Weft knitting, electrospinning and 3D printing; single layer weft-knitting coil structure bare stent</td>
<td>Good structural and molding effects and possess tissue-matched mechanical properties, good biocompatibility and biodegradability; probability of aseptic inflammation</td>
<td>[16, 21, 23, 32]</td>
</tr>
<tr>
<td>CS/GHA/heparin</td>
<td>Freeze-drying, 3D printing; fibers, powders, 3D printed structures and sponges</td>
<td>Appropriate immune response, mild antigenic properties, and good hemostatic properties; insufficient mechanical strength</td>
<td>[44]</td>
</tr>
<tr>
<td>dECM</td>
<td>Freeze-drying, 3D printing and decellularized tissue engineering</td>
<td>Biocompatibility and biodegradability; insufficient mechanical strength</td>
<td>[4]</td>
</tr>
</tbody>
</table>
Natural biological scaffolds are gaining increasing attention due to their appropriate immune response, mild antigentic properties, and good hemostatic properties [41]. However, natural scaffolds often lack the mechanical properties required for an ideal tissue repair scaffold and need to be modified with other compounds, such as galactose. Typically, natural scaffolds are fabricated in the form of fibers, powders, 3D printed structures, and sponges [42]. Chitosan is an excellent candidate for hemostatic scaffold synthesis due to its antimicrobial and hemostatic properties. Studies have shown that the addition of hydrophobic groups to chitosan enhances its anti-infective and hemostatic strength through solid hydrophobic interactions with platelet membranes, erythrocytes, and bacteria [43]. These findings suggest that the CS/GHA/heparin scaffold could be a potential candidate for liver tissue engineering [44].

![Scaffold Shapes](image)

Fig. 3: Natural scaffold shapes: fibers, sponges, powders, 3D printed and decellularized tissues [42]

Despite the widespread use and rapid development of various tissue-engineered scaffolds, such as natural and synthetic polymers, their repair capacity is often limited by challenges in overcoming immunogenicity, mimicking the in vivo microenvironment, and exhibiting mechanical or biochemical properties similar to those of natural organs/tissues. Fortunately, the emergence of decellularized extracellular matrix (dECM) scaffolds provides a new approach to overcome these obstacles and is considered ideal for functional organ/tissue regeneration [45]. Exciting research results in stem cell, biomaterials engineering, and nanobiotechnology are expected to revolutionize liver regenerative medicine. The function and survival of hepatocytes rely on cell-cell interactions and attachment to ECM assemblies. Biological scaffolds can serve as a support platform for cell growth, proliferation, and differentiation, and can mimic physiological conditions that promote cell growth and differentiation, ultimately leading to liver regeneration. In combination with genetic engineering, mock liver tissue systems have great potential as powerful tools for efficient in vitro stem cell expansion and maintenance of mature function, supporting future personalized transplantation approaches.

### 2.6 Pancreatic Duct Stents

Chronic pancreatitis often presents with pancreatic duct obstruction and dilation due to pancreatic stenosis and stones, resulting in increased pancreatic duct pressure. The main treatment method for this condition is endoscopic retrograde cholangiopancreatography (ERCP) pancreatic...
duct stenting, supplemented by pancreatic duct dilatation and stenosis dilation, with a pain relief rate of over 70% [46].

Non-biodegradable plastic pancreatic duct stents are commonly used in clinical practice due to their affordability and simplicity in surgical operation. Plastic pancreatic duct stents exhibit good stability and low rejection rates, but they have limitations such as inability to adapt to the physiological bending of the pancreatic duct and the need for surgical removal at a later stage. Itoi et al. [47] reported a new ultrasound endoscopically guided plastic stent with a total length of 20 cm and an effective length of 15 cm, featuring two internal flanges at each end, which potentially reduces the risk of stent displacement.

Biodegradable stents offer high biocompatibility and biodegradability, eliminating the need for surgical removal after insertion, and significantly reducing hospitalization duration, cost, and surgical risks [48]. Cahen et al. [49] inserted a new biodegradable stent with a diameter of 6.0 mm and a length of 3.0-4.0 mm in seven patients with chronic pancreatitis. The expected degradation time was 3-6 months. After 6 months, all patients underwent ERCP, and all stents degraded in all patients. One patient required a second plastic stent placed after 3 months, two patients underwent surgery, and the remaining four patients experienced significant relief of pancreatic duct stenosis symptoms within 1 year. Therefore, it was concluded that the new biodegradable stent can effectively relieve pancreatic duct stenosis in chronic pancreatitis, degrade completely in the short term, and is safe to use. Maoen et al. [50] 3D printed a radiopaque polychitosan-palladium sulfate stent using an extrusion-based molding technique. However, due to the properties of polychitosan, it could not be 3D printed using heat treatment, and the polychitosan stent prepared by freeze-drying technique was unsuitable for pancreatic ductal stents due to its irregularity and large porosity. This is because the irregularity and coarse porosity may result in leakage of pancreatic fluid from the sides of the stent, corroding the tissue. The authors immersed poly(chitosan)-palladium sulfate stents with different molecular weights in simulated pancreatic fluid in vitro, periodically measured changes in mass, water absorption, and mechanical properties, and verified their biocompatibility, degradability, and impermeability linearity through in vivo and in vitro tests. The results showed that the poly(chitosan)-palladium sulfate stents prepared using this method exhibited good structural and molding effects, possessed tissue-matched mechanical properties, and demonstrated good biocompatibility and impermeability linearity.

Currently, plastic pancreatic duct stents and metal pancreatic duct stents are more commonly used in clinical practice, despite their limitations such as the risk of pancreatic injury and stent displacement. However, with the advancement of science and technology, these limitations are being gradually addressed through innovative improvements in traditional pancreatic duct stents. Biodegradable stents have shown promising results in relieving pancreatic duct stenosis in chronic pancreatitis, as they can degrade completely within a specified period of time, are simple and safe to use, and hold great potential for the future.

3 Conclusion

Digestive tract stents are increasingly being used in clinical practice. To achieve better treatment outcomes, researchers are exploring ideal stents made from suitable materials using various preparation methods. Currently, stent research has evolved from single bare metal stents to combination stents with drug-loading functions such as mechanical expansion of the digestive tract, targeted therapy, inhibition of tumor tissue, and loading of growth factors or cells to enhance bio-
compatibility and cell proliferation rates. Researchers are designing and manufacturing suitable stents to meet the treatment requirements of different diseases.

However, there are still limitations in the application of stents, such as bleeding, perforation, stent displacement or obstruction, and recurrent obstruction caused by tumor ingrowth. There is also ongoing controversy regarding the ideal characteristics of stents, including length, diameter, and type. Several important properties of gastrointestinal stents for clinical use, such as mechanical properties, biodegradability, biocompatibility, and multifunctional properties like drug elution and biodegradability, need to be carefully considered.

Emerging technologies such as 3D printing and acellular tissue engineering hold great potential as new solutions for gastrointestinal disorders. In the future, breakthroughs can be expected in the manufacturing technology of tissue engineering stents that mimic the natural structure of the digestive tract. Additionally, advancements in stem cell research and nanobiotechnology are anticipated to bring revolutionary changes to tissue engineering and regeneration.

In order to continue advancing the research and development of digestive tract stents, multidisciplinary teams with expertise in biomaterials, digital technology, textiles, and medical clinics must collaborate and innovate together to develop increasingly effective types of digestive tract stents, bringing hope to patients with digestive tract diseases.

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