

# CANCER THERAPY



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# Cytosponge: A breakthrough in detection of barrett's esophagus

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## Abstract

Barrett's esophagus or BE is a very worst condition of GERD. It is the disease, which associated with gastroesophageal reflux. In this disease normal tissues of esophagus changes to tissues like intestine. This disease does not have any specific symptoms in early stage. But in fatal stage the symptoms may like to the symptoms related to GERD. As time increases this disease may produce the sever oesophageal adenocarcinoma. Cytosponge is a very effective and new treatment strategy for this Barret's oesophagus disease [1-3]. The mechanism of action of cytosponge is very simple and it is having some advantageous points over endoscopy and surgery. In this review, we have tried to draw a scientific approach about Berret's esophagus [4-7] and the use of cytosponge to treat this disease.

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## Introduction

Cancer is a unique disease, which means abnormal cell proliferation with having the potential to spread over the whole body. There are generally two types of tumours, one is benign tumour, and another is malignant tumour. Cancer is generally the formation of malignant tumours. Cancer cells are having several significant features among them the most important is inhibition of the programmed cell death or apoptosis. There are several reasons for cancer. The most important cause is exposure of human into the carcinogenic environment.

It is reported in2015, about 90.5 million people was suffering from cancer. About 14.1 million new cases occur a year (not including skin cancer other than melanoma). It caused about 8.8 million deaths (15.7% of deaths). The major types of cancer that are very common in case of male are lung cancer, prostate cancer, colorectal cancer and stomach cancer. In females, the most common types are breast cancer, colorectal cancer, lung cancer and cervical cancer. In children the most common type of cancer are acute lymphoblastic leukemia, brain tumours and non-Hodgkin lymphoma.



## Signs and symptoms

Actually, early signs and symptoms of cancer is not so much significant. Signs and symptoms appear as the function of the time and fatalness of the diseases. Though the general signs and symptoms are lump formation, abnormal bleeding, prolonged cough, unexplained weight loss, and a change in bowel movements [8,9]. These are the very general symptoms, and these may be a cause of another disease. Cancer can be detected by some screening tests. It is typically investigated by medical imaging and confirmed by biopsy.

## Causes

The principle cause of cancer is the changes of DNA within the cells. The change in the structure of DNA is known as the mutation and the causing agent is known as mutagen. DNA is made up of large number of genes and each genes contain a specific information. Changes in DNA leads to the change in genes and errors in genes can cause the cell to stop its normal function and this may convert a cell to cancerous one.

According to American Cancer Society general causes for cancer are - Smoking and Tobacco, Diet and Physical Activity, Sun and Other Types of Radiation, Viruses and Other Infections. If we go for some detail then we will find that tobacco, alcohol, obesity, poor diet, lack of physical activity, viral attack, environmental pollutants, radiation etc. are important for causing cancer.

The major treatments for cancer are radiation therapy, surgery, chemotherapy, and targeted therapy or combination of the above treatments.

## Esophageal cancer

Esophagus is also known as food pipe. It is the pipe that connects pharynx and the stomach. It is the main passage that convey the food from mouth to stomach by peristaltic movement [10,11].

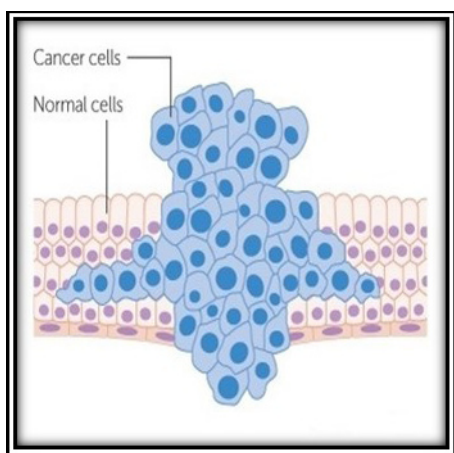


Figure 1: Cancer cell and normal cell

Esophageal cancer is having two sub-type of diseases. These are

## Esophageal Squamous-Cell Carcinoma (ESCC)

- This type of oesophageal cancer is relatively more frequent in the developing countries.
- It is arising from the epithelial cells of the oesophagus.

## Esophageal Adenocarcinoma (EAC):

- It is more frequent in developed countries.
- It comes from glandular cells present in the esophagus.

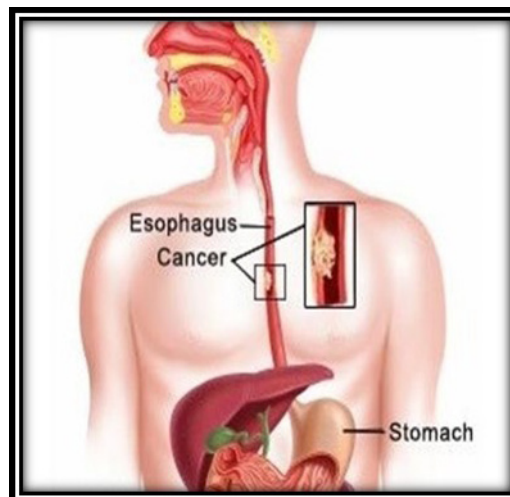


Figure 2: Esophageal cancer

## Signs and symptoms

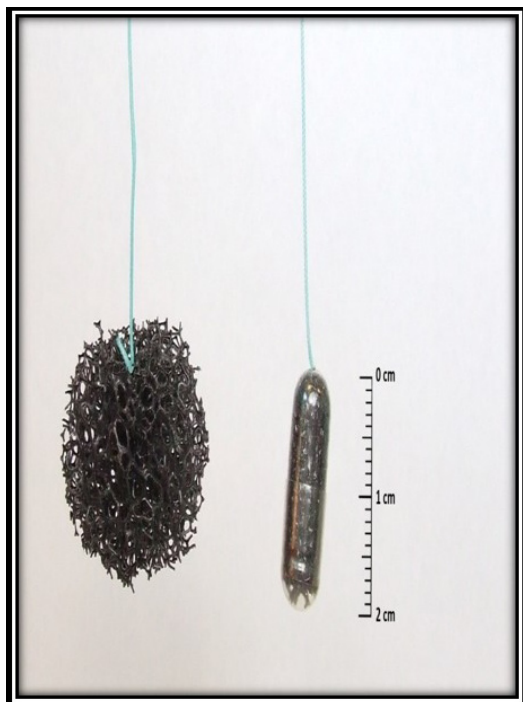
During the very first stage, there is no such prominent symptoms to identify the disease. But the symptoms become more prominent when the disease spread over 60% of the circumference of the oesophageal tube. At this stage tumour goes to its advanced form. Onset of symptoms is usually caused by narrowing of the tube due to the physical presence of the tumour.

The most frequent symptom is difficulty in swallowing. This may happen with softer foods, liquid foods, and solid foods. Pain is common with difficulty in swallowing. Weight loss is often an initial symptom. Reduced appetite and undernutrition lead to weight loss. Another common symptom is pain behind the breastbone or in the region around the stomach often feels like heartburn. Administered of food or anything which is going to be swallowed may increase the pain.

## Cytosponge cell collection kit

The Cytosponge cell collection kit consists of the following things as shown in Figure 5.

The Cytosponge (Medtronic GI Solutions) is a single-use device used to collect cells from the lining of the esophagus.



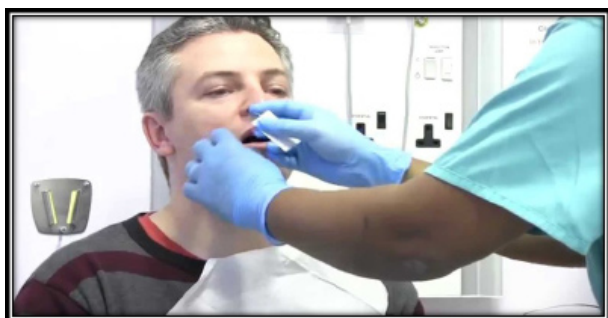
**Figure 3:** Cytosponge dimensions



**Figure 4:** Cytosponge cell collection kit

Cytosponge cell collection unit is having a small mesh sponge. The diameter of the sponge is about 30 mm. It contains gelatine capsule and the capsule is attached to a string (Figure 4). Generally, it is taken with sufficient amount of water and when the cytosponge reaches to the stomach then the gelatin part dissolves.

#### Application of cytosponge on patients



**Figure 5:** Patient application of Cytosponge

Generally, it is given to the patients with sufficient amount of water and the gelatin part disappears when cytosponge reaches to the stomach. A lidocaine throat spray may be used to reduce the minor discomforts during application of the cytosponge. After near about five minutes, the observer retrieves the expanded sponge. As it is retrieved, the slightly abrasive mesh collects cells along the length of the esophagus. Two most anticipated physical concerns include swallowing the Cytosponge and extracting it.

#### Swallowing the sponge

At the time of very beginning, patients imagine that the capsule may be bigger in size. Patients get really surprised when they handle cytosponge. Actually, cytosponge is having the similar size of the tablets of regular taking and this incident assures the patients that the cytosponge capsule will not create.

#### Extracting the sponge

After exposure to the expanded Cytosponge some patients said that it was rougher than they expected. As a result, they worried that the expanded cytosponge may damage their oesophagus. Some people also think that they would gag or vomit the Cytosponge. A consistent concern was the possibility of the string breaking and the Cytosponge being stuck in the oesophagus or stomach.

#### Video reassurance

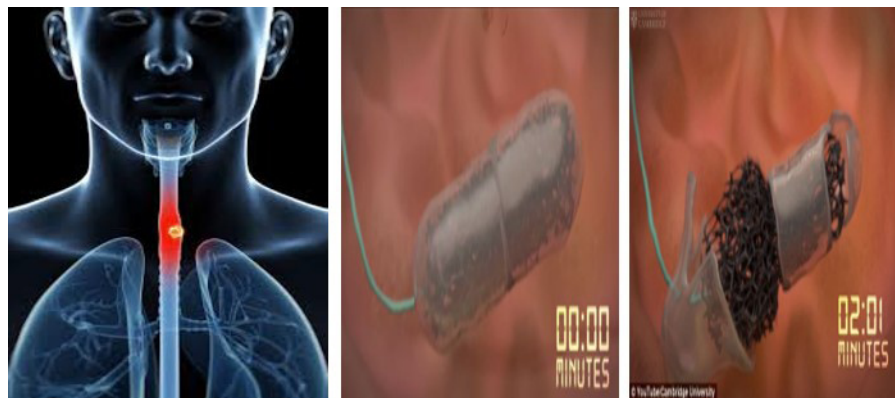
When patients watch the videos, they express more positive attitude towards the cytosponge administration. The main reason for this attitude shift was because the extraction of the sponge was considerably quicker than expected. The fact the patient did not gag during its extraction was considered comforting.

#### Mechanism of action of cytosponge:

The Cytosponge test for the detection of esophageal cancer takes place in the following way:

- The patient swallows the pill.
- The 'Cytosponge' sits within a pill, which is swallowed.
- The pill when it enters the stomach dissolves. The gelatin shell opens up in the stomach and reveals a sponge. this takes about 5minutes time
- After 5mins, the string that is attached to the Cytosponge is pulled up.
- As the string travels up the esophagus, it collects the cells lining the esophagus. About a million of cells can be captured in its honeycomb like matrix of the sponge.
- The cells are isolated and tests are performed to determine whether the cells are malignant or normal.

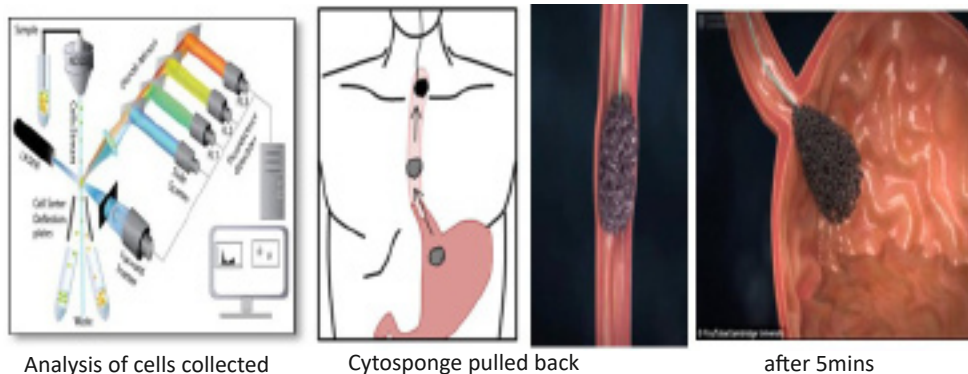
In this way, Cytosponge can be used to determine malignant or premalignant conditions potentially and effectively in a more comfortable manner.



Pill swallowed by patient

Cytosponge in the GIT

Gelatin shell dissolves



Analysis of cells collected

Cytosponge pulled back

after 5mins

**Figure 6:** Schematic of the mechanism of action of Cytosponge

**Comparison with endoscopy**

While the Cytosponge test is not intended to replace endoscopy, it was felt that the new device was preferable physically, practically and economically.

**Discomfort**

In most of the cases several patients feel unpleasant experience when they undergone endoscopies for their heartburn. And cytosponge test is having no such disadvantages. It is more comfortable.

**Practical factors**

And there is one interesting fact regarding cytosponge that it is more quicker procedure than endoscopy and does not require anaesthetic.

The fact that people would be able to resume their everyday activities immediately after the procedure was also seen as a benefit.

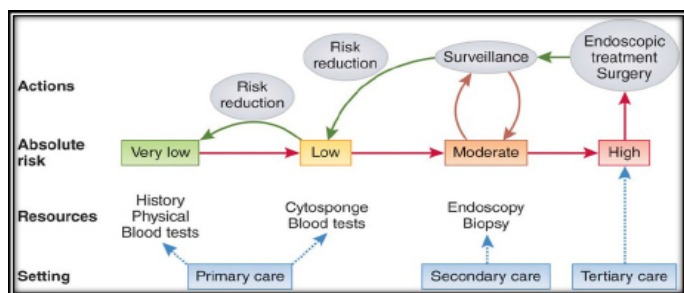
**Economic factors**

A minority of people considered the superior cost-effectiveness of the Cytosponge test, and the benefits this would have for the healthcare system. The Cytosponge test hence was found to be acceptable physically, practically and economically, as well as being preferred to endoscopy[12,13].

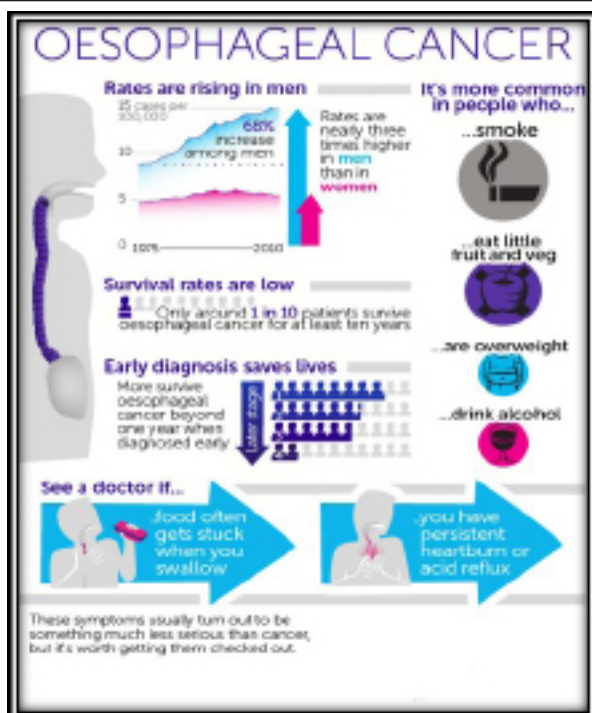
**Conclusion**

Esophageal adenocarcinoma is developed from the Barrett esophagus or Barrett’s esophagus (BE). Alternatively, we can say that Barrett esophagus is the precursor of esophageal adenocarcinoma. So, patients with having BE can be identified and handled carefully so that the risk of development of adenocarcinoma is minimum. And if it is necessary then abnormal cells should be removed to reduce the risk.

Available treatments like endoscopy and biopsy are the standard one for identifying BE. But the problem is that they are quite expensive. And sometimes they procedure uncomfortable experiences to the patients.



**Figure 7:** Comparison between Cytosponge test and endoscopy



**Figure 8:** Risk of oesophageal cancer and Steps to be taken if suspected

Cytosponge is a small sponge having small mesh size. And this sponge is situated within a soluble gelatin capsule. And the capsule can be safely administered by oral route. And with combination of some biomarker analysis, the Cytosponge is having a good sensitivity and specificity for detecting individuals likely to have BE.

Use of the Cytosponge with biomarker analysis could improve identification of individuals with BE through a test that is less onerous for patients than endoscopy, as well as less costly.

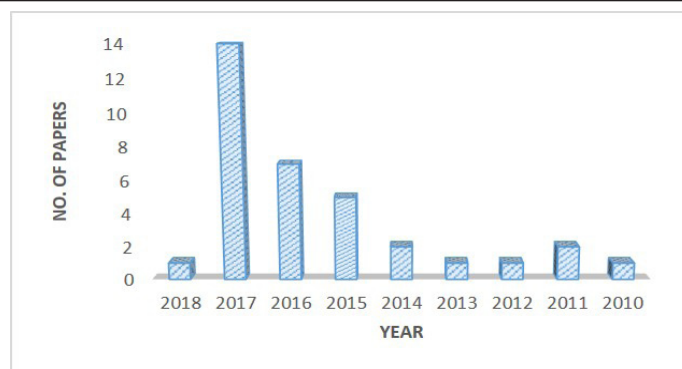
Compared with diagnostic biopsy, the Cytosponge procedure was 79.9% sensitive and 92.4% specific for diagnosing Barrett's esophagus, according to an online report, January 29th in PLOS Medicine.

"The Cytosponge test is safe and generally acceptable to patients with symptomatic reflux or dyspepsia undergoing investigation, and for those patients with Barrett's esophagus undergoing surveillance", the researchers conclude.

Proper investigation and research in this field could help Cytosponge test become a most effective, comfortable technique for the early detection of esophageal cancer.

#### Future prospect

Barrett's oesophagus is such a critical condition, which may lead to the formation of oesophageal adenocarcinoma. This oesophageal adenocarcinoma is a very high lethal tumour. The incidence of spreading barrett's oesophagus [14] followed by the oesophageal adenocarcinoma has been increased in the western world over the last past three decades. In near pasts there have been tremendous advancements done in the field of the treatment of Barrett's oesophagus [15,16] And several treatment strategies have been taken to treat the premalignant tumours.



**Figure 9:** A graphical plot of the increasing research activities on cytosponge test

The above data plots clearly say that, cytosponge is gaining numerous interests day by day for the treatment of Barrett's oesophagus disease. And there are so many researches are going on in this matter. This clearly indicates that cytosponge have taken the attention of the researchers. And that is leading to the numerous modifications of the cytosponge. Research activities are going on. Patient education and awareness will lead to further approach of this method of esophageal cancer detection. Therefore, if investigated properly and research continues then it may be an alternative to endoscopy ensuring a more painless, comfortable method in the early detection of Adenocarcinoma.

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