



## Cerebrovascular Disease

### The third leading cause of death in Japan: Finding the answers to the treatment of cerebrovascular disease

Cerebrovascular disease (stroke) kills approximately 110,000 people each year, making it the third leading cause of death in Japan\*.

\* MHLW, 2017 demographic statistics (determinate number)

Stroke can be roughly divided into hemorrhagic cases including subarachnoid hemorrhage which is caused by rupture of the cerebral aneurysm, and ischemic cases causing cerebral infarction due to a thrombus. Both hemorrhagic and ischemic cases may cause paralysis, language disorder, and motor dysfunction, which results in long-term nursing care, becoming bedridden, or death.

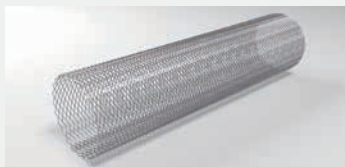
Minimally invasive advanced medical care has developed over the past decade. This contributes to reduced physical and mental burden for a wider range of stroke patients and improves their QOL after recovery.

### The age of post-platinum coils

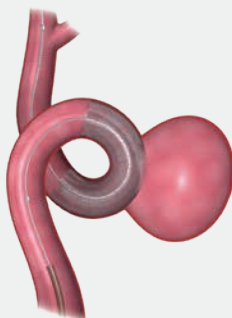
The first treatment developed and introduced as a minimally invasive procedure for cerebrovascular disease was cerebral aneurysm coil embolization (endovascular treatment) that treats or prevents ruptured cerebral aneurysms. Unlike conventional craniotomy, endovascular treatment uses a catheter that is inserted into the blood vessel and guides a thin, soft spiral platinum coil to the cerebral aneurysm. This treatment fills the cerebral aneurysm with the coil to stop the blood inflow into the aneurysm and prevent bleeding from the rupture of aneurysm. This treatment introduced to Japan in 1997 became a forerunner of minimally invasive treatment.

However, performing coil embolization on an aneurysm which has a wide entrance (neck) was very difficult. To that end, adjunctive stents were introduced in Japan in 2008. Adjunctive stents were developed for the purpose of preventing protrusion or deviation of the coil mass from the parent artery during coil embolization, even when the aneurysm entrance is wide.

In 2015, flow diverters, the first stent-like device for treating cerebral aneurysms, were introduced in Japan. These devices made it possible to treat large and giant aneurysms (only for aneurysms with a maximum 10mm diameter and 4mm neck, and excluding rupture acute phase aneurysms), which had been defined as difficult-to-treat cerebral aneurysms. Such difficult-to-treat cases are as follows: even with treatment, blood flow into the cerebral aneurysm cannot be fully blocked, and hence cannot be completely cured; and re-treatments are necessary because measures to prevent cerebral aneurysm are not effective. Flow diversion is a new treatment method; while preserving the original blood flow of arteries, blocking the blood inflow to the cerebral aneurysm, proliferating endothelial cells at the neck of the blocked cerebral aneurysm to induce the formation of a new tunica intima, and reducing



Flow diverters for cerebral aneurysm treatment



the risk of cerebral aneurysm ruptures. However, its placement is limited to sites from petrous part of internal carotid artery to the upper and lower petrous part, and the treatment is very difficult. Therefore, as of June 2019, the treatment with flow diverters is performed at limited facilities in Japan.

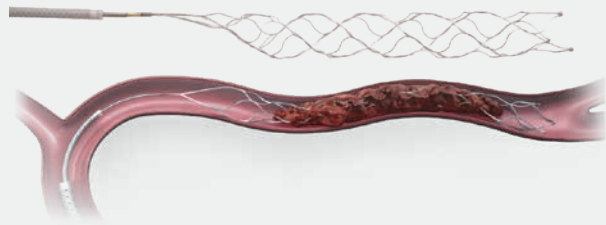
### New treatment options for cerebral infarction

For acute cerebral infarction, which is the most common type of stroke, there are two therapies: internal therapy of intravenous t-PA treatment, and thrombus collection therapy which uses a thrombectomy device. Thrombectomy therapy was first introduced in Japan in 2008. Since then, we have seen a decade of innovation in thrombectomy. In general, acute cerebral infarction develops in the middle of the night or in the morning, and the onset timing is often not clear. The t-PA cannot be used in some cases because of the body constitution and treatment of other diseases.

In 2010, as a new treatment option for acute cerebral infarction, a soft, wire thrombectomy device with a spiral tip was launched for the first time in Japan. This enabled treatment of those patients who were unresponsive to t-PA (internal treatment) within 8 hours of the onset of acute cerebral infarction, or those who were not eligible for internal treatment. The results of clinical studies showed that 70% to 80% of occluded blood vessels are reopened with endovascular treatment for acute cerebral infarction using this device.

In 2011, approval was given to a device that collects thrombi while breaking them down with a catheter equipped with a powerful aspiration pump. Then in 2014, a stent-type thrombectomy device was introduced, and this improved reopening rate and safety.

In 2019, more than 10 years after the introduction of the first thrombectomy device, the indication of the device was expanded; treatment within 8 hours after the onset was expanded to treatment within 24 hours after the onset for some stent-type thrombectomy devices. This also allowed the expansion of treatment options to include those patients who might have suffered serious sequelae as they had not been eligible for this device, such as those with unknown onset times or those who presented with cerebral infarction symptoms upon arising in the morning.



Thrombectomy devices for the treatment of acute cerebral infarction

### The next 10 years

In the last 10 years, endovascular treatment for cerebrovascular disease has evolved and allowed patients to have more treatment options. According to Stroke Treatment Guidelines 2015 (Supplement 2017), it is highly recommended that patients diagnosed with acute cerebral infarction be treated with mechanical thrombectomy within 6 hours of the onset in addition to the conventional medical treatment (Grade A). Going forward, endovascular treatment is expected to become the standard treatment for an increasing number of patients.