

Self-Expanding Platinum-Coated Nitinol Devices for Transcatheter Closure of Atrial Septal Defect: Prevention of Nickel Release

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ABSTRACT: Background. A variety of nitinol-containing devices for transcatheter closure of atrial septal defects (ASD) has been widely used. However, there is concern about the release of nickel after nitinol device implantation. In this study, a platinum-coated nitinol device was braided from nanoplatinum-coated nitinol wires in order to prevent nickel release. The serum nickel levels before and after device implantation and the 1-year results were evaluated. **Methods.** Thirty-one patients, aged 4–59 years, and weighing 13.7–90.0 kg, underwent transcatheter closure. Blood samples for serum nickel levels were taken before, 1 day, 1 week, 1 month and 3 months after implantation. **Results.** Twenty-nine (93.6%) patients had a successful implantation. The mean ASD diameter was 19.7 ± 4.8 mm (range 10–30 mm). Procedure-related complications included transient brachial plexus injury in 1 patient, and transient dysrhythmia in 4 patients. All 29 patients had complete closure within 1 month after implantation. The mean serum nickel levels at baseline and at 1 day, 1 week, 1 month and 3 months after implantation were 0.65 ± 0.28 , 0.63 ± 0.18 , 0.67 ± 0.34 , 0.55 ± 0.16 , 0.52 ± 0.14 ng/ml, respectively. There was no significant difference in serum nickel levels before and after implantation. There were no device-related complications at 1-year follow up. **Conclusions.** Transcatheter ASD closure using a platinum-coated nitinol device can be performed safely and successfully with good outcomes. Nano-coating of platinum on nitinol wires can prevent nickel release following device implantation.

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Key words: atrial septal defect; transcatheter closure; platinum-coated nitinol device; nickel release

Nitinol, an alloy composed of 55% nickel and 45% titanium, has been widely used in medical products. With its superelastic and shape-memory properties, nitinol has generated new models of occlusion devices for transcatheter closure of atrial septal defects (ASD) and various other cardiovascular defects. These nitinol devices not only yielded excellent results, but also made for easy and safe device implantation.

However, there is a concern about release of nickel after implantation of nitinol devices,^{1,2} especially in patients with nickel allergy.^{3–5} This is where platinum-activation of nitinol by nanotechnology has a role. By a process called plasma deposition, ultra-thin layers of platinum atoms are deposited on the surface of nitinol wires. The platinum layers prevent nickel release, but do not change the superelastic and shape-memory properties of nitinol. This concept has produced a new ASD occlusion device model that should resolve the nickel release problem.

The purpose of this study was to evaluate the 1-year results of platinum-coated nitinol device use in percutaneous transcatheter closure of ASDs and to study the difference in serum nickel levels before and after ASD closure with this device.

Methods

The study protocol and informed consent form were approved by the ethics committee of the Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. All patients or their guardians gave written consent for their participation in the study.

Patient population. Patients > 3 years of age who had a secundum ASD and right ventricular volume load by transthoracic echocardiography (TTE) and in whom defect closure was indicated were invited to participate in the trial. Patients were excluded who had associated cardiac defects that needed open-heart surgery and in whom TTE demonstrated an ASD size > 30 mm and septal rims < 7 mm from the right pulmonary vein, coronary sinus, superior vena cava, inferior vena cava and mitral valve.

Device design. The device was braided from platinum-coated nitinol wires into 2 circular discs (acting as left and right atrial discs) with a central connecting waist (stenting at the ASD), and filled with 3 circular polypropylene sheaths (each was sewn at the rim of the right atrial disc, the central connecting waist and the left atrial disc, respectively) to enhance thrombogenicity (Figure 1). Although the structure of the device appears similar to the Amplatzer septal occluder (AGA Medical, Golden Valley, Minnesota), the surface composition of the nitinol wires that was platinum coated, including the fabric used for occlusion, are different. The loading system consisted of a small tube that acted as a loader and a delivery cable that could be connected with the device by

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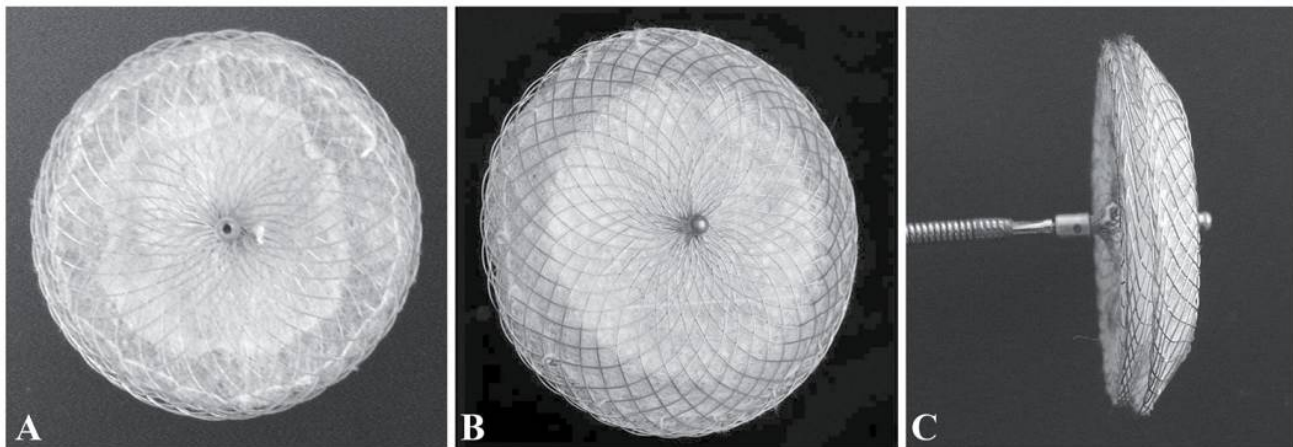


Figure 1. The atrial septal defect closure device. (A) Frontal view of the right atrial disc; (B) frontal view of the left atrial disc; (C) side view with the left atrial disc on the right and the right atrial disc on the left (the right atrial disc is connected to the delivery cable).

screw connection. Because the platinum layers did not interfere with the superelastic and shape-memory properties of the nitinol, the device that was connected to the delivery cable could be easily pulled and collapsed in the loader. The device that was prepared in the loading system was loaded into a long vascular sheath and deployed at the ASD. The size of the device is indicated as the diameter of the central connecting waist. In our previous animal experiment using a swine model, we demonstrated safe and successful outcomes with this device. The post-mortem finding showed complete neo-endothelialization over the surface of the device on both the right and left atrial discs at 6 weeks after implantation.⁶

Transcatheter closure technique. The entire procedure was performed under general anesthesia, with a transesophageal echocardiographic study (TEE) and fluoroscopic control. The patient was given heparin 100 units/kg and a single dose of intravenous cefazolin 50 mg/kg (maximum dose of 2 gm) as a prophylactic antibiotic. ASD size and morphology were assessed by TEE. The device size was selected according to the stretched diameter of the ASD indicated by the diameter of the sizing balloon that stopped left-to-right flow across the ASD. In the cases where balloon sizing was not done, device deployment was attempted according to the size of the ASD diameter by TEE plus 4 mm. The selected device that was attached to the delivery cable was collapsed in the loader and introduced into the long sheath. Using fluoroscopic and TEE guidance, the device was deployed for ASD closure with the central waist of the device stenting at the ASD, and both the left and right atrial discs attaching to both sides of the atrial septum. If the device position and alignment, as assessed by TEE and fluoroscopy, were not adequate, the device was retrieved and exchanged for a new one that was larger or smaller than the previous device, as determined by the operator. Once satisfactory device position and stability were achieved, the delivery cable was unscrewed to detach from the deployed device.

To avoid oversized device implantation, a balloon-assisted technique was applied in large ASD cases, requiring a

different deployment technique using a balloon angioplasty catheter to assist in alignment of the device during deployment. The balloon supported the left atrial disc and prevented it from prolapsing into the right atrium (Figure 2).

Follow up and laboratory analysis. Between July 2005 and May 2006, 31 patients (10 males and 21 females) underwent attempted transcatheter ASD closure. There were 20 pediatric and 11 adult cases. The ages ranged from 4 to 59 years, with a median age of 11 years. The patients' weight ranged from 13.7–90 kg, with a median weight of 33 kg.

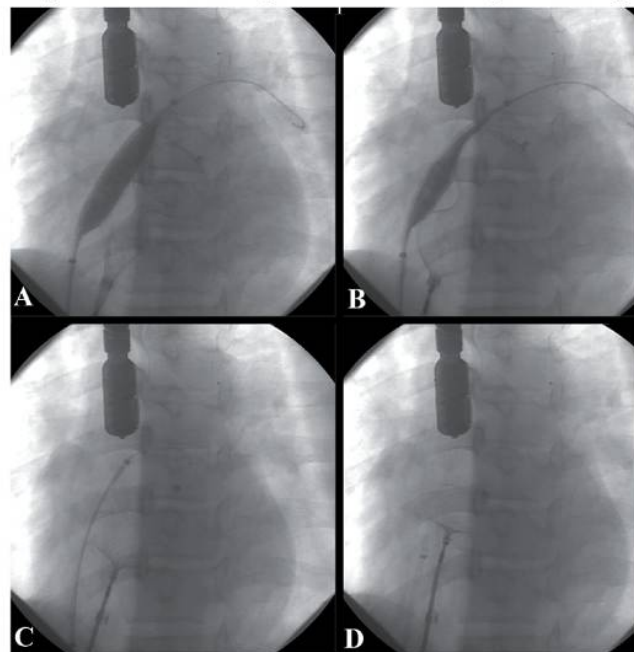


Figure 2. A 15 mm balloon valvuloplasty catheter was used to assist in the deployment of the 30 mm ASD device in a 14-year-old girl who had a 26 mm ASD as measured by TEE. (A) The balloon was inflated first and then the left atrial disc was deployed, followed by partial deployment of the right atrial disc. (B) The right atrial disc was fully deployed with simultaneous gradual balloon deflation. (C and D) While the right atrial disc was pushed toward the left atrial disc to flatten the device, the balloon catheter was gently pulled back to the right atrium.

Antiplatelet therapy after device implantation included clopidogrel 1 mg/kg/day in pediatric cases, or 75 mg/day in adult cases for 1 month, combined with aspirin 3–5 mg/kg/day in pediatric cases, or 300 mg/day in adult cases for 6 months. Clinical information,

including a TTE study, was evaluated at 1 day, 1 week, 1 month, 3 months, 6 months and 1 year after device implantation. Blood samples for serum nickel analysis were collected before device implantation and at 1 day, 1 week, 1 month and 3 months after implantation. The blood was centrifuged immediately and the serum collection was frozen at -20°C until analysis was performed. Serum nickel levels were also analyzed in 100 normal populations for comparison with the baseline before implantation. Serum nickel analysis was conducted by electrothermal atomic absorption spectrophotometry (ETAAS) with Zeeman background using Varian Spectra AA 220 (Varian Australia Pty Ltd., Mulgrave, Victoria, Australia) and Zeeman background equipped with a GTA 110 graphite furnace and a PSD-100 autosample.

Statistical analysis. Data were expressed as mean $\pm$ standard deviation. For comparison of the serum nickel values at 1 day, 1 week, 1 month and 3 months after device implantation with the baseline before implantation, statistical analysis was performed using the paired t-test. The difference between the serum nickel levels in the patients and those in the normal populations was analyzed using the independent samples t-test. A p -value < 0.05 was considered statistically significant.

Results

Device deployment was successful in 29/31 patients (93.6%). One patient, a 50-year-old female, had dislodgement of the device to the left atrium during the procedure which required emergent surgery for device removal and ASD closure. The other patient, a 15-year-old female, experienced device deployment failure and underwent subsequent elective surgical ASD closure. The ASD size measured by TEE in 29 cases ranged from 10–30 mm, with a mean size of 19.1 ± 4.5 mm. The device size ranged from 14–34 mm, with a mean size of 23.5 ± 4.6 mm. Balloon sizing was performed in 19 patients. The mean stretched ASD diameter by sizing balloon was 20.8 ± 5.4 mm, and the implanted device size in the 19 patients was 22.1 ± 5.2 mm. The balloon-assisted technique

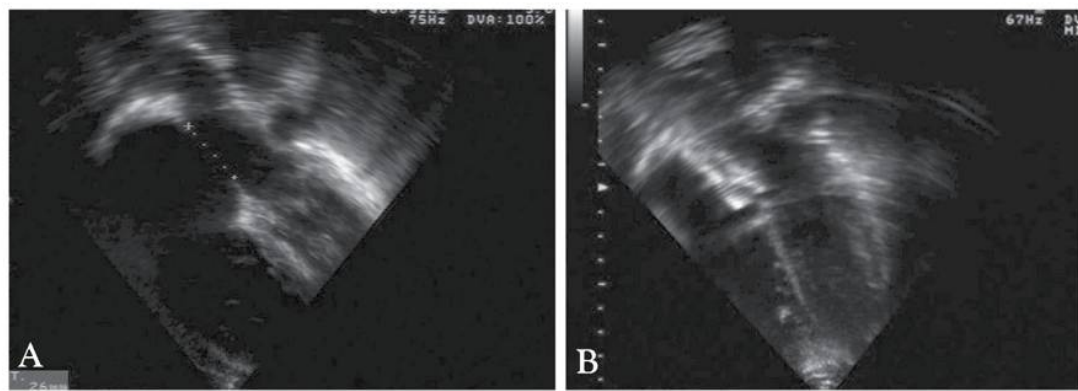


Figure 3. Echocardiographic study in a 26 mm atrial septal defect case that was closed with a 30 mm device (the same patient as in Figure 2). (A) Preimplantation; (B) 6 months post implantation.

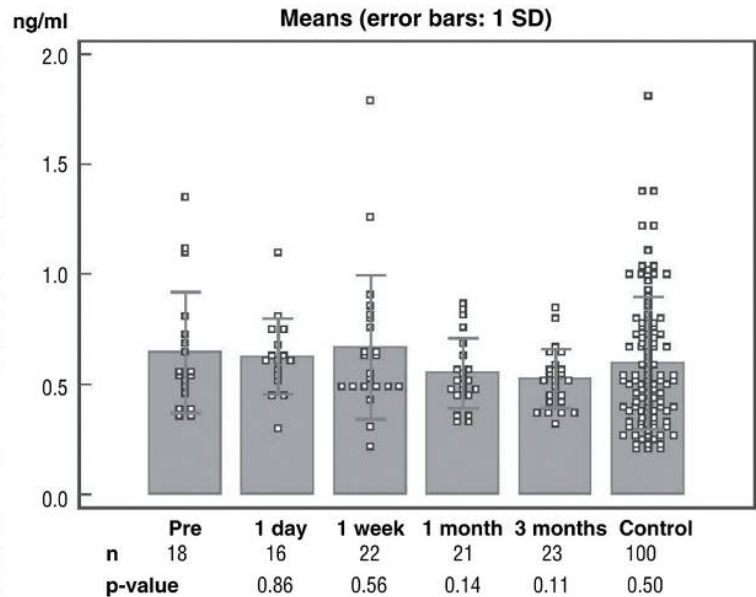


Figure 4. Serum nickel levels at pre-and post-implantation. (n = number of cases in each group; p-value = the p-value as compared to the mean level at baseline).

was applied in 7 children and 2 adults. Procedure-related complications included transient brachial plexus injury in 1 patient, transient complete heart block in 1, and transient junctional rhythm in 3 patients.

Clinical information and serial TTE follow up (Figure 3) at 1 day, 1 week, 1 month, 3 months, 6 months and 1 year after implantation revealed no device-related complications. The complete closure rate by TTE was 58.6% (17 cases), 82.8% (24 cases) and 100% (29 cases) at 1 day, 1 week and 1 month after implantation, respectively. One patient, a 4-year-old girl who had 2 ASDs (10 and 4 mm, respectively, by TEE), underwent implantation with a 14 mm device for closure of the larger defect. The patient had complete closure of the larger defect at 1 week after implantation, but still had residual flow across the smaller defect at 1-year follow up. Two patients complained of frequent episodes of ecchymosis when given their antiplatelet medication.

Twenty-five patients underwent serial blood sample collection for serum nickel analysis, but only 18 of them had a baseline level. The mean serum nickel levels at baseline ($n = 18$) and at 1 day ($n = 16$), 1 week ($n = 22$), 1 month ($n = 21$), and 3 months ($n = 23$) after implantation were 0.65 ± 0.28 , 0.63 ± 0.18 , 0.67 ± 0.34 , 0.55 ± 0.16 , and 0.52 ± 0.14 ng/ml, respectively. Serum nickel concentrations at baseline and post implantation, using the paired t-test, were not statistically different before and after device implantation. *P*-values were 0.86 (versus 1 day, $n = 15$), 0.56 (versus 1 week, $n = 17$), 0.14 (versus 1 month, $n = 15$), and 0.11 (versus 3 months, $n = 17$). The mean serum nickel level in the 100 normal populations was 0.60 ± 0.30 ng/ml. The patients' mean baseline level was also not significantly different from that in the normal population (*p*-value = 0.5), as shown in Figure 4. Patient blood samples (pre- and post implantation), when compared with those from the normal population, showed no statistically significant difference in mean serum nickel levels (*p*-value = 0.90).

Discussion

Nitinol-containing devices for transcatheter closure of atrial septal defects (ASDs) have been used worldwide over the past decade. With its excellent shape memory and superelasticity, nitinol has made ASD closure safe, easy and successful. According to recent reports, the Amplatzer ASD occluder, a self-expandable nitinol-containing device, has been widely used and has yielded excellent outcomes.⁷⁻¹⁰ This study was our first experience with transcatheter ASD closure. We had a successful implantation rate of 93.6%. However, all of our successful cases had complete closure by TTE within 1 month and had no device-related complications at 1-year follow up. One of our patients experienced transient brachial plexus injury due to overstretch of the arm during the procedure, which recovered completely within 1 week. One of our patients, a 5-year-old girl who weighed 13.7 kg and had an ASD size of 17 mm by TEE and 18 mm by balloon sizing, experienced transient complete heart block. We first chose an 18 mm device to close the defect, but this failed. We then retrieved it and exchanged it for a 22 mm size device, but the patient developed complete heart block immediately after implantation. Finally, the 22 mm device was retrieved and changed to a 20 mm device, which was well-positioned and aligned. After the procedure, the patient had normal sinus rhythm.

Dalvi et al described a balloon-assisted technique for closure of large ASDs with the Amplatzer septal occluder by using a Meditech sizing balloon catheter to stabilize the device during deployment.¹¹ To avoid an oversized device, we applied the balloon-assisted technique in those cases where the device could not be loaded by the usual technique. Applying the same concept, we used an angioplasty balloon catheter to support the left atrial disc, resulting in successful deployment.

Some reports in the literature demonstrated evidence of nickel release after Amplatzer ASD occluder implantation. Ries et al described a significant rise in serum nickel levels

after Amplatzer device implantation. The mean serum nickel level significantly increased at 24 hours, had a maximum threefold increase at 1 month, and declined to the baseline level at 6 months after implantation. No adverse effects from increased nickel levels were found.¹ Burian et al also demonstrated a significant rise in both serum and urine nickel levels after implantation of an Amplatzer ASD occluder. The serum nickel levels increased up to fivefold from baseline during the 6-week postimplantation period. However, serum and urine concentrations returned to baseline levels within 4–6 months post implantation.² The nickel release after implantation of nitinol-containing devices may induce reaction in the patients, especially in those with nickel allergy. Fukahara et al reported systemic reaction that developed in a 37-year-old female 2 months after patent foramen ovale (PFO) closure with a nitinol-containing Cardia PFO-Star occluder (Cardia, Inc, Burnsville, Minnesota). Skin patch testing demonstrated hypersensitivity for nickel. Her symptoms completely resolved after the device was explanted 4 months post transcatheter closure.³ Singh et al demonstrated skin reactivity after 12 hours of a skin patch test with the Amplatzer septal occluder in a 54-year-old female ASD patient who had a history of potential nickel allergy. The patient experienced cutaneous erythema and swelling after the patch was removed and developed blistering of the skin for the next 24 hours. With the negative reactivity to the patch test using the CardioSEAL device (Nitinol Medical Technologies, Boston, Massachusetts), the patient underwent successful ASD closure using the CardioSEAL device.⁴ Lai et al demonstrated clinical findings of pericarditis in a 38-year-old male who underwent PFO closure with the Amplatzer PFO occluder device. Allergy patch testing showed a Type IV hypersensitivity reaction to nickel. His symptoms improved over a 3-week period while on prednisolone.⁵

In our study, the ASD occluder device was braided from platinum-coated nitinol wires. The platinum coating prevents nitinol exposure and nickel release. Our patients did not develop any device-related complications, including potential nickel allergic reaction, at 1-year follow up. Serum nickel analysis showed no significant difference in nickel levels before and after device implantation. Compared to the normal population, nickel levels, both before and after implantation, did not statistically differ from the controls, a finding that supports the notion that nickel release is prevented by nano-coating the surface of nitinol wires with platinum layers.

Conclusion

Transcatheter ASD closure using a self-expandable platinum-coated nitinol device can be performed safely and successfully with good results. There was no evidence of nickel release after implantation.

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References

1. Ries MW, Kampmann C, Rupprecht HJ, et al. Nickel release after implantation of the Amplatzer occluder. *Am Heart J* 2003;145:737-741.
2. Burian M, Neumann T, Weber M, et al. Nickel release, a possible indicator for the duration of antiplatelet treatment, from a nickel cardiac device in vivo: A study in patients with atrial septal defects implanted with an Amplatzer occluder. *Int J Clin Pharmacol Ther* 2006;44:107-112.
3. Fukahara K, Kazutomo M, Riess N, et al. Systemic allergic reaction to the percutaneous patent foramen ovale occluder. *J Thorac Cardiovasc Surg* 2003;125:213-214.
4. Singh HR, Turner DR, Forbes TJ. Nickel allergy and the Amplatzer septal occluder. *J Invasive Cardiol* 2004;16:681-682.
5. Lai DW, Saver JL, Araujo JA, et al. Pericarditis associated with nickel hypersensitivity to the Amplatzer occluder device: A case report. *Catheter Cardiovasc Interv* 2005;66:424-426.
6. Lertsapcharoen P, Khongphatthanayothin A, La-orkhun V, et al. Self-expanding nanoplatinum-coated nitinol devices for atrial septal defect and patent ductus arteriosus closure: A swine model. *Indian Heart J* 2006;58:315-320.
7. Masura J, Gavora P, Formanek A, Hijazi ZM. Transcatheter closure of secundum atrial septal defects using the new self-centering Amplatzer septal occluder: Initial human experience. *Cathet Cardiovasc Diagn* 1997;42:388-393.
8. Chan KC, Godman MJ, Walsh K, et al. Transcatheter closure of atrial septal defect and interatrial communications with a new self expanding nitinol double disc device (Amplatzer septal occluder): Multicentre U.K. experience. *Heart* 1999;82:300-306.
9. Masura J, Gavora P, Podnar T. Long-term outcome of transcatheter secundum-type atrial septal defect closure using Amplatzer septal occluders. *J Am Coll Cardiol* 2005;45:505-507.
10. Wang JK, Tsai SK, Wu MH, et al. Short- and intermediate-term results of transcatheter closure of atrial septal defect with the Amplatzer septal occluder. *Am Heart J* 2004;148:511-517.
11. Dalvi BV, Pinto RJ, Gupta A. New technique for device closure of large atrial septal defects. *Catheter Cardiovasc Interv* 2005;64:102-107.