


Percutaneous endovascular biopsy for the diagnosis of pulmonary artery masses: A preliminary study of single-center

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Abstract

Percutaneous endovascular biopsy (PEB) including forceps biopsy and catheter aspiration has been used to make a pretreatment diagnosis for pulmonary artery (PA) masses. This retrospective study aims to describe the procedure of PEB and compare the diagnostic yield of forceps biopsy and catheter aspiration for a definite diagnosis in patients with PA masses. All consecutive 22 patients (53 ± 14 years), 11 males and 11 females, who underwent PEB for pathologic confirmation between November 2018 and November 2022 were enrolled. All 22 patients performed computed tomography pulmonary angiography or positron emission tomography-computed tomography to confirm the filling defects suspicious for PA malignancy before intervention. And then, all patients underwent PEB successfully without acute or fatal complications, including both forceps biopsy and catheter aspiration in 15 cases, only forceps biopsy in 5 cases, and only catheter aspiration in 2 cases. Histopathological analysis provided a definite diagnosis in all PEBs with a clinical success of 91.0% (20/22). Among them, in 15 patients who underwent both forceps biopsy and aspiration biopsy, the technical success using forceps biopsy was 93.3% (14/15), and aspiration biopsy was 6.7% (1/15), and there was a significant difference in diagnostic accuracy when comparing two techniques. Twenty-one out of 22 PA masses (95.5%) were malignant, of which, the most frequent malignant lesion observed was PA sarcoma (66.7%, 14/21). Benign lesion included one thrombus (4.5%, 1/22). In conclusion, PEB is an effective and safe diagnostic method for differentiating benign and

Abbreviations: CI, cardiac index; CTPA, computed tomography pulmonary angiography; DAP, dose area product; EBUS-TBNA, endobronchial ultrasound-guided transbronchial needle aspiration; FDG-PET/CT, fluorodeoxyglucose positron emission tomography/computed tomography; mPAP, mean pulmonary arterial pressure; mRAP, mean right atrial pressure; MRI, magnetic resonance imaging; PA, pulmonary artery; PAS, pulmonary artery sarcoma; PEB, percutaneous endovascular biopsy; PVR, pulmonary vascular resistance; TE, tumoral embolism.

Cheng Hong and Jie-Long Lin contributed equally to this study.

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malignant PA masses and could be performed when PA masses appeared clinically malignant.

KEYWORDS

catheter aspiration, endovascular biopsy, forceps biopsy, intravascular filling-defect, pulmonary artery

INTRODUCTION

The pulmonary artery (PA) may be involved by different primary and secondary tumors, such as primary pulmonary artery sarcoma (PAS) and tumoral embolism (TE), manifested as an intravascular filling-defect lesion on imaging. However, those PA malignancies can be misdiagnosed as thrombotic lesions due to its unspecific clinical and radiologic findings, leading to misdiagnosis, delayed treatment, and even death.¹⁻³ Moreover, both prognosis and therapeutic options vary drastically for PAS, TE, and pulmonary thromboembolism. For example, the prognosis of PAS is extremely poor and the median survival time of untreated PAS is less than 2 months.⁴ Early and accurate diagnosis in conjunction with timely intervention is the key to prolong survival time.

Noninvasive imaging methods including computed tomography pulmonary angiography (CTPA), magnetic resonance imaging (MRI), and fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) can help to distinguish PA malignancy from pulmonary thromboembolic disease, but remain uncertainty about identifying the underlying pathology,⁵⁻⁸ thus, the final definite diagnosis is achieved only by pathological examination. However, the histological examination of most cases is confirmed by an intraoperative surgical biopsy. Early acquisition of tumor specimens is essential to establish a definitive diagnosis and plan the appropriate treatment. Several methods of tumor tissue sampling including CT-guided transthoracic biopsy and endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) have been described.^{6,9,10} But these procedures are often difficult to perform when the lesion is located in the PA.

Percutaneous endovascular biopsy (PEB) including forceps biopsy and catheter aspiration is a mini-invasive intervention method, directly approaching the lesions in the vascular cavity, which may be a reasonable diagnostic method for patients with suspected malignant PA masses. Due to the rarity of PA malignancies, evidence regarding PEB is limited to a small series of cases and case reports.¹¹⁻¹⁴

The aim of this study was to assess the efficiency of PEB and to compare forceps biopsy with catheter aspiration in the diagnosis of PA masses and to report our experience.

MATERIALS AND METHODS

Patient population

From November 2018 to November 2022, 23 consecutive patients underwent PEB for confirming the nature of PA mass at our institution. Before PEB, imaging studies including CTPA and/or PET-CT were performed to characterize PA masses and assess its anatomical relationship to nearby structures. Our institutional review committee approved the study and written informed consent of the patient was obtained before PEB. During PEB, 15 of the patients underwent right heart catheterization to obtain baseline hemodynamic data.

PEB procedure

The operation process of PEB was shown in Figure 1. PEB was performed through the right femoral vein using a 6-F 11-cm introducer sheath. Heparin sodium (50 U/kg) was injected after insertion of the sheath, and another 1000 units was injected 1 h later. Using a 0.035-in. guidewire (RADIFOCUS® GUIDE WIRE M, TERUMO®), a 5-F pigtail catheter (PIG 145° INFINITI®, Cordis®) was inserted into the main PA through the introducer sheath. PA angiography was performed according to the location of the lesion. After that, The sheath was exchanged for an 8-F 65-cm vascular introducer sheath (REF CL-07780 Super Arrow-Flex; ARROW) with guidewire. In 3 patients, an 8-F multi-purpose catheter (MPA 1; Cordis) was used, which was later replaced an 8-F vascular introducer sheath (Super Arrow-Flex; ARROW) in the other 20 patients (Figure 2). An endomyocardial biopsy forceps device (2.2 mm × 50 cm, 7-F Maxi-Curved; Argon Medical Devices) was gently advanced up with both stainless steel hinged

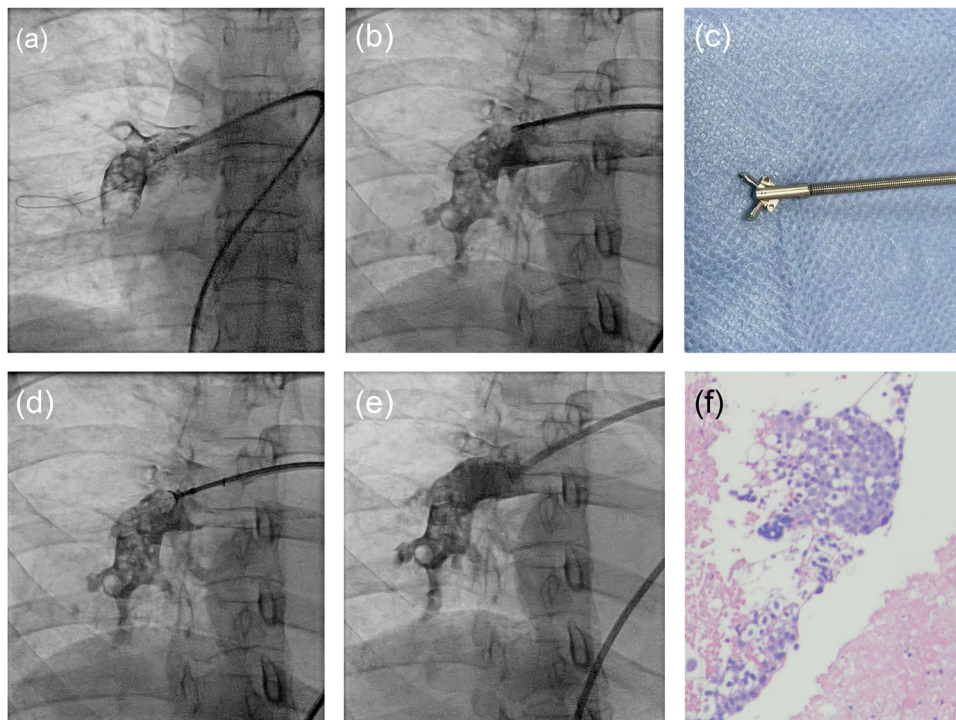


FIGURE 1 The operation process of PEB. (a) The 8-F vascular introducer sheath was put in close touch with tissue in the filling defect according to angiography. (b) Multiangle angiography to determine the relative position of the sheath and the lesion. (c) Endomyocardial biopsy forceps (2.2 mm × 50 cm, 7 F Maxi-Curved; Argon Medical Devices). (d) Under fluoroscopic guidance, the biopsy device was advanced outside the introducer tip and subsequently gently placed on the mass to obtain the tissue sample. (e) After the procedure, a second pulmonary angiography confirmed the absence of vascular injury. (f) Right pulmonary artery mass tissue obtained by biopsy forceps and the final histological findings was TE by choriocarcinoma. PEB, percutaneous endovascular biopsy; TE, tumoral embolism.

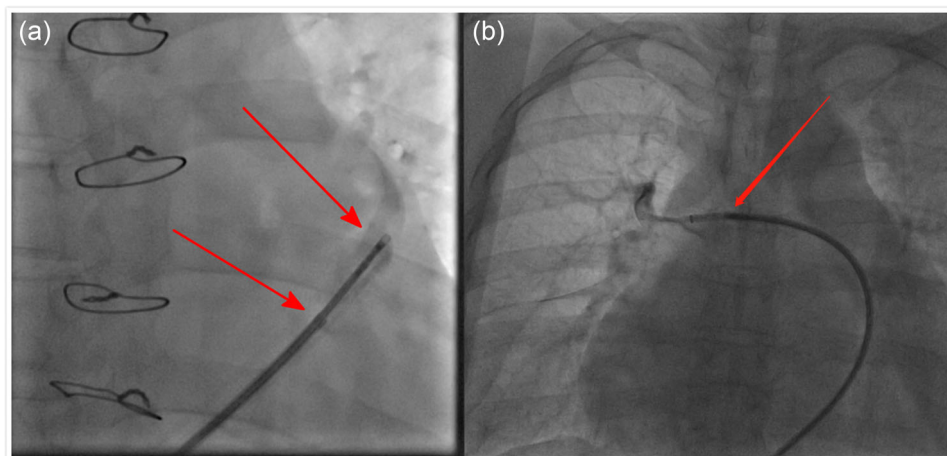


FIGURE 2 The difference between 8-F MPA catheter and 8-F vascular introducer sheath. (a) The biopsy forceps can just pass through the 8-F MPA catheter (outer diameter of 2.7 mm; inner diameter of 2.2 mm; Cordis). And the biopsy forceps needed to be sent outside the tip of the catheter for angiography to determine the location of the biopsy forceps (red arrow). (b) The 8-F vascular introducer sheath (inner diameter of 2.87 mm, Super Arrow-Flex; Arrow) with a large space between the biopsy forceps and the sheath. Angiography can be directly performed to confirm that the tip of the introducers is adjacent to the mass without pulling back the introducer sheath (red arrow). MPA, main pulmonary artery.

cutting jaws in the closed position. During the period, angiography was performed as needed to confirm real-time operation. Under fluoroscopic guidance, the biopsy device was advanced outside the introducer tip with the hinged jaws in the open position and subsequently gently placed near the mass. Once resistance was sensed, quickly clamped the tissue and then pulled out the biopsy forceps device. Repeated biopsy was performed until at least three specimens were obtained. After clamping, a 50-mL syringe connected to the 8-F sheath was used for vacuum suction. Suction was repetitively performed three or more times to obtain a sufficient amount of specimens. The specimens were sent to perform hematoxylin-eosin and immunohistochemical staining for pathological evaluation. After the procedure, a second PA angiography was performed to exclude vascular injury.

Data relating to PA lesion characteristics, diagnostic yield, and safety was recorded and analyzed. All patients were followed up until December 31, 2022 to obtain a definitive diagnosis or the diagnosis was verified by other standard techniques, such as EBUS-TBNA or surgery.

Statistical analysis

The data were expressed as mean values \pm standard deviation or median (25% quantile, 75% quantile) based on the distribution of data. The McNemar's test and κ test were performed to compare the diagnostic yield and concordance between forceps biopsy and catheter aspiration, respectively. Data was analyzed using the statistical software SPSS 25.0 (SPSS, Inc.). $p < 0.05$ was considered to indicate a statistically significant difference.

RESULTS

PEB was performed by the same operator on all 23 patients without complications such as bleeding and perforation during the perioperative period of PEB. One patient was excluded from the study due to the uncertain diagnose obtained by PEB and could not be further verified. Thus, the final study population included 22 patients (11 males and 11 females) with a mean age of 53 ± 14 years (range 26–76 years). The clinical characteristics, PEB-related information and final diagnosis of the patients are presented in Tables 1 and 2. The clinical symptoms of the patient were nonspecific and the main manifestations were chest pain, shortness of breath, cough, and hemoptysis. The locations of filling-defect lesion mainly included both main pulmonary artery (MPA) trunk and bilateral pulmonary artery (BPA)

TABLE 1 Clinical characteristics of the patients.

Variable	All patients (N = 22)
Age (years)	53 ± 14
Gender (male/female, n)	11/11
Main symptoms (n)	
Chest pain	8
Shortness of breath	8
Cough	7
Hemoptysis	7
Fever	3
Chest tightness	1
Dyspnea	1
Imaging before PEB (n)	
CTPA/PET-CT	16
CTPA	6
Site of tumor (n)	
MPA + BPA	10
MPA + RPA	1
BPA	2
LPA	3
RPA	6
Histopathologic diagnosis (n)	
PAS	14
TE	3
Poorly differentiated carcinoma	1
EHE	1
Myeloid sarcoma	1
Chondrosarcoma	1
CTEPH	1

Abbreviations: BPA, bilateral pulmonary artery; CTEPH, chronic thromboembolic pulmonary hypertension; CTPA, computed tomography pulmonary angiography; EHE, epithelioid hemangioendothelioma; LPA, left pulmonary artery; MPA, main pulmonary artery; PAS, pulmonary artery sarcoma; PET-CT, positron emission tomography-computed tomography; RPA, right pulmonary artery; TE, tumoral embolism.

($n = 10$), right PA (RPA) ($n = 6$), and left PA (LPA) ($n = 3$). Of the 22 cases enrolled in the study, a definitive histological diagnosis was made in 20 cases (20/22, 90.9%) through tissue sampling with forceps biopsy and/or catheter suction, of which, a definite diagnosis could be reached in 14 cases with the combination of both forceps biopsy and catheter aspiration, 5 cases with only forceps biopsy, and 1 case with only catheter aspiration. While the remaining two cases (2/22, 9.1%) had a

definitive diagnosis through other diagnostic procedures including EBUS-TBNA and surgery. Histopathologic results included 14 cases of PAS, 3 cases of TE, 1 case of poorly differentiated carcinoma, 1 case of epithelioid hemangioendothelioma, 1 case of myeloid sarcoma, 1 case of chondrosarcoma and 1 case of chronic thromboembolic pulmonary hypertension. Specific diagnostic information of each patient is specified in Supporting Information: Table S1.

Table 3 shows the baseline hemodynamics and radiation exposure information of patients. Overall, the dose area product (DAP) was 903.5 (511.6–2178.0) uGym² and the

total contrast agents used per PEB procedure was 100.5 ± 59.3 mL. The mean pulmonary arterial pressure (mPAP) was 30.2 ± 10.4 mmHg, pulmonary vascular resistance (PVR) was 3.0 ± 0.9 Wood units, and cardiac index (CI) was 5.5 ± 3.2 L/min/m², indicating that most patients had mild to moderate pulmonary hypertension at baseline.

With regard to the diagnostic accuracy in 15 cases who underwent both forceps biopsy and catheter aspiration, the diagnostic yield of forceps biopsy was 93.3% (14/15), and catheter aspiration was 6.7% (1/15). There was a significant difference in diagnostic accuracy when comparing two techniques (Table 4). But the κ value was 0.010, indicating slight agreement.

TABLE 2 PEB-related information.

Variable	All patients (n = 22)
Definite diagnosis with PEB (n/total n, %)	
with forceps biopsy	(19/20, 95.0%)
with catheter aspiration	(2/17, 11.8%)
Baseline hemodynamics (n = 15)	
mRAP (mmHg)	9.3 ± 7.5
mPAP (mmHg)	30.2 ± 10.4
CI (L/min/m ²)	5.5 ± 3.2
PVR (Wood units)	3.0 ± 0.9
Radiation exposure	
DAP, overall (uGym ²)	903.5 (511.6–2178.0)
Total contrast agents used per PEB procedure (mL)	100.5 ± 59.3

Abbreviations: CI, cardiac index; DAP, dose area product; mPAP, mean pulmonary arterial pressure; mRAP, mean right atrial pressure; PEB, percutaneous endovascular biopsy; PVR, pulmonary vascular resistance.

TABLE 3 Established diagnosis by forceps biopsy and/or catheter aspiration in the study patients.

Diagnosis	Forceps biopsy and catheter aspiration (n = 15)	Only forceps biopsy (n = 5)	Only catheter aspiration (n = 2)
Malignant lesions	13	5	1
PAS	8	4	0
Metastasis			
TE	3	0	0
Others	2	1	1
Benign lesions	1	0	0
CTEPH	1	0	0
No definitive diagnosis	1	0	1

Abbreviations: CTEPH, chronic thromboembolic pulmonary hypertension; PAS, pulmonary artery sarcoma; TE, tumoral embolism.

DISCUSSION

Due to the aggressiveness and poor prognosis of PAS and other PA malignancies, early diagnosis and intervention are vital. However, these tumors have similar clinical and radiological findings as a thrombotic lesion, frequently leading to misdiagnosis with an acute pulmonary embolism or chronic thromboembolic pulmonary hypertension. Imaging techniques such as CTPA or PET-CT can demonstrate the features of PA mass and help to distinguish between malignant and benign entities, but final diagnosis often remains unclear when only based on imaging findings alone. In this situation, to obtain accurate pathological results can guide clinical treatment more effectively. Meanwhile, it would be helpful if the diagnosis could be made before surgical intervention. In case of surgery, it can avoid an intraoperative frozen section, thus reducing the cardiopulmonary bypass time.

	Diagnostic yield		p Value	κ value
	Forceps biopsy	Catheter aspiration		
Definite diagnosis	93.3%	6.7%	<0.001	0.010

TABLE 4 Diagnostic yield of forceps biopsy and catheter aspiration ($n = 15$).

However, obtaining the pathological specimens of PA lesions is often challenging. When the tumor does not invade the extravascular tissues, it is very difficult to obtain pathological evidence at an early stage. In the confirmed cases reported previously, most of the pathological evidence was obtained by surgery, while a few relied on minimally invasive methods to obtain pathological tissue. Because the mass is located in the PA, CT-guided transthoracic biopsy is often associated with a risk of bleeding. Some cases of successful diagnosis using EBUS-TBNA have been described in the literature. EBUS-TBNA is also a relatively less invasive, less time-consuming intervention with no risk of radiation exposure. It allows real-time sampling of lesions and reflects the blood flow and stenosis of PA. However, as described in our study, most patients have mild to moderate pulmonary hypertension. Pulmonary hypertension caused by proximal PA obstruction can lead to bronchial artery hypertrophy, which can increase the risk of bleeding during EBUS-TBNA procedures. From this perspective, PEB is a safe and efficient alternative procedure. Recent small case-series studies^{10–14} have described PEB techniques including forceps biopsy and catheter aspiration to obtain endovascular tumor tissue samples for definitive diagnosis. In this retrospective study, we reviewed the results of forceps biopsy and catheter aspiration and compared the success rate of the two methods. Overall, PEB has a high technical success rate with a diagnostic accuracy of 91.0% (20/22). And the forceps biopsy was superior to catheter aspiration ($p < 0.001$). This could be due to the ability of the forceps biopsy to sample more mass tissue.

During the operation of forceps biopsy, the biopsy forceps can be used for multiple times to ensure that the real cores of tissue can be obtained. In PAS, tumor tissue is often covered by thrombus in situ and necrotic tissue.¹² In our study, only thrombus tissue through forceps biopsy was obtained in a patient (Supporting Information: Table S1), but the patient was finally diagnosed as PAS. Therefore, a problem with forceps biopsy is that a single clamp may not obtain enough tumor tissue and may miss the tumor. In our experience, to improve the positive rate, repeat biopsies can be performed to obtain multiple pieces of tissue for pathological examination. Meanwhile, the results of PEB should be considered in combination with clinic and radiology, such as PET-CT, to avoid misdiagnoses in patients with PA lesions.

Endovascular aspiration biopsy is an alternative approach for obtaining tumor-associated clots, but with limited success.¹⁴ In our study, 17 patients underwent aspiration biopsy, only 2 cases got histologic tumor diagnosis (11.8%), and 15 cases for negative results. We analyzed that it might be related to the nature of the tumor, when the surface of the mass was fibrous and hard, and suction could not be appropriately performed.¹⁰ In addition, because catheter aspiration is not directly clamped, the positive rate may be low, and this may also lead to poor concordance between the two technical methods. Therefore, during the operation, we should pay attention to the selection of diseased vessels without blood flow and distal occlusion and observe the properties of the aspirate. If the aspirate is a thrombus or necrotic substance, the position where the catheter enters should be adjusted, when operating again to improve the positive rate.

During the operation of PEB, there are some specifics deserve our attention. To improve the quality of biopsy specimens, the introducer sheath should be placed adjacent to mass and be stabilized in this position when the biopsy device advanced to the target lesion. We can evaluate the precise position of the biopsy forceps device in real time under fluoroscopy and contrast-enhanced imaging. In 3 patients, we used a 90-cm 8-F MPA guiding catheter with an inner diameter of 2.2 mm, which just allowed the biopsy device to pass through. The biopsy forceps needed to be sent outside the tip of the catheter for angiography in order to determine the location of the biopsy forceps; otherwise, the angiographic images were not clear. In the other 20 patients, we opted to use an 8-F vascular introducer sheath (inner diameter of 2.87 mm) with a larger space between the biopsy forceps and the introducers, so there is no need to pull back the introducer sheath to perform angiography (Figure 2) and the 8-F sheath with better flexibility could easily pass through the curved PA.

Although our experience did not cause acute or delayed complications, it has to be admitted that this technique has the risk of bleeding, perforation, and pseudoaneurysm. But the real risk of these complications has not been established. It is worth noting that the clamped or aspirated tumor tissue may fall off and locally implant to form dissemination. For patients with PAS originating from the vascular intima, and the operation is also in the vascular lumen, the possibility of implantation and dissemination is small. Because the location and type

of PA tumors are heterogeneous, and early diagnosis and appropriate treatment can also help control and prevent disease progression, so the risk of metastasis caused by PEB still needs to be further explored. In addition, for patients with almost complete obstruction of the main PA, we do not recommend PEB. If the tissue falls off, it may completely block the PA.

Another possible disadvantage of PEB is radiation exposure. Radiation exposure in our study was recorded as 903.5 (511.6–2178.0) uGym² and the overall amount of contrast agent is 100.5 ± 59.3 mL. However, most patients in our institution undergo right heart catheterization before PEB. And the radiation dose in PEB procedures may vary depending on the complexity of the procedure and the skills of the operator. Therefore, it is necessary to further explore the radiation dose obtained from PEB.

Because of the rarity of this disease, one major limitation of this retrospective study is the small number of enrolled patients. And the small sample size of this study makes it difficult to draw a definitive conclusion on the superiority of forceps biopsy and catheter aspiration. In the future, a multicenter, larger patient cohort may be necessary.

CONCLUSION

In summary, we have found that PEB is a useful and safe technique of endovascular tissue sampling in PA. And it should be performed in time when the PA malignancy is suspected to give the best diagnostic yield.

AUTHOR CONTRIBUTIONS

Study design, drafting, and revising manuscript: Cheng Hong and Hai-Ming Chen. *Acquisition of data:* Xiao-Feng Wu. *Analysis and interpretation of data:* Hai-Ming Chen and Jie-Long Lin. *Critical revision of the manuscript for important intellectual content:* Wen-Liang Guo and Xiao-Yan Li. All authors approved the final version of the manuscript to be published.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this article.

ETHICS STATEMENT

This study was approved by the institutional review committee of the First Affiliated Hospital of Guangzhou Medical University (NO. 2021-K-36) and written informed consent of the patient was obtained before PEB.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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