### **CLINICAL STUDY**

# Transcatheter Arterial Chemoembolization with Spherical Embolic Agent in Patients with Pulmonary or Mediastinal Metastases from Breast Cancer

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#### **ABSTRACT**

**Purpose:** To evaluate safety and feasibility of transcatheter arterial chemoembolization with superabsorbent polymer microspheres (SAP-MS) for patients with pulmonary or mediastinal metastasis from breast cancer.

**Methods:** Between November 2002 and January 2015, 14 patients with 29 unresectable pulmonary or mediastinal breast cancer metastases underwent transcatheter arterial chemoembolization using SAP-MS (50–100 μm) after injection of a combination of 2–4 types of anticancer drugs (eg, cisplatin [30 mg] + fluorouracil [500 mg], or epirubicin [40 mg] + mitomycin C [4 mg] + fluorouracil [500 mg]). As a primary endpoint, local tumor response and adverse events were evaluated 1 month after the first transcatheter arterial chemoembolization, according to Response Evaluation Criteria In Solid Tumors Version 1.1 and Common Terminology Criteria for Adverse Events Version 4 criteria. Transcatheter arterial chemoembolization was repeated as needed. Overall survival was analyzed as a secondary endpoint.

**Results:** Response rate was 28.6% (partial response, 4 patients; stable disease, 10 patients). Median progression rate was -12.7%. No cases of hematologic toxicity of grade 3 or higher were observed. A grade 3 maculopapular rash was observed in 1 patient. After the first transcatheter arterial chemoembolization sessions, 63 additional transcatheter arterial chemoembolization sessions were performed (average, 5.5 sessions per patient; range, 2-10 sessions). The median overall survival time after the first session was 29 months, and the 5-year survival rate was 49.5%.

**Conclusions:** Transcatheter arterial chemoembolization with SAP-MS is a well-tolerated and feasible palliative treatment option for patients with pulmonary or mediastinal metastasis from breast cancer.

#### **ABBREVIATIONS**

BA = bronchial artery, MBC = metastatic breast cancer, PA = pulmonary artery, PD = progressive disease, RR = response rate, SAP-MS = superabsorbent polymer microspheres

Metastatic breast cancer (MBC) occurs in 25%–40% of patients with primary breast cancer (1). Although hormone therapy, molecular targeted therapy, and systemic chemotherapy are widely accepted as standard clinical treatments

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for MBC, the prognosis of MBC is still poor (2). According to the algorithm for MBC reported by Hortobagyi et al (3), the best therapeutic option for patients with chemotherapy-refractory disease or patients who are intolerant to chemotherapy is best supportive care. However, if breast metastases to mediastinum and hilum are not treated, they may enlarge and cause life-threatening conditions, such as superior vena cava syndrome, bronchial infiltration, and hemoptysis (4). To prevent these oncologic emergencies, therapies that induce rapid tumor shrinkage are required. Although some studies reported lobectomy for the treatment of metastatic lung tumors, this therapeutic option is invasive and associated with high mortality (5–8).

In addition to oncologic emergencies, patients with pulmonary metastases usually have severe dyspnea, cough, and pain caused by cancer progression (9). Therefore, they require continuous and repeated sessions of treatment. Transpulmonary chemoembolization has been described as a treatment for metastatic lung tumors (10-13). However, it is not effective for mediastinal tumors. Studies have demonstrated both in vivo and in vitro that the feeding arteries for metastatic lung tumors include not only the pulmonary artery (PA) but also the bronchial artery (BA) and nonbronchial systemic arteries (14-17). In addition, the BA anatomically supplies the mediastinal and hilar lymph nodes as well as lung metastases (17). The biggest difference between transpulmonary chemoembolization and transcatheter arterial chemoembolization is that transcatheter arterial chemoembolization can treat mediastinal and hilar lymph node metastases as well as lung metastases. However, to the authors' knowledge, very few studies have been published to date on transcatheter treatment from bronchial and nonbronchial systemic arteries for pulmonary metastases. The aim of this study was to retrospectively evaluate the safety and feasibility of transcatheter arterial chemoembolization for pulmonary and mediastinal metastasis from breast cancer.

#### **MATERIALS AND METHODS**

#### **Patient Characteristics**

This study was approved by the institutional review board, and informed consent was obtained from all patients. Between November 2002 and January 2015, 32 patients with pulmonary and/or mediastinal metastasis from breast cancer underwent TACE. Indications for transcatheter arterial chemoembolization were follows: (i) refractory to, intolerance to, or rejection of standard systemic chemotherapy; (ii) no or well-controlled brain metastasis; (iii) no other life-threatening diseases; (iv) no active infection; (v) Eastern Cooperative Oncology Group performance status of  $\leq 3$ ; (vi) not pregnant or breastfeeding; and (vii) not allergic to contrast material. The following 18 patients were excluded from the study: 3 patients with a tumor < 2 cm, 10 patients with pneumonia or atelectasis, and 5 patients in whom follow-up contrast-enhanced computed tomography (CT) was not performed within 1 month after transcatheter arterial chemoembolization.

The study included 14 female patients with a median age of 58.5 years (range, 37–77 y). Patient characteristics are shown in **Table 1**. Of patients, 1 underwent metachronous bilateral mastectomy, 7 underwent unilateral total mastectomy, 5 underwent unilateral partial mastectomy, and 1 refused all standard therapies including surgery. Types of tumors included solid tubular carcinoma (6 patients), invasive ductal carcinoma (2 patients), and scirrhous-type carcinoma (2 patients); 4 patients had an unknown type. Seven patients had no extrathoracic tumors, and the other 7 patients had local recurrence or other organ metastases, such as in the axillary lymph nodes, liver, brain, and bones. Of the 14 patients, 10 had tumors that were refractory to systemic chemotherapy, 3 were intolerant

Table 1. Patient Characteristics	
Characteristic	Value
Number of patients	14
Age, y, median (range)	58.5 (37–77)
Type of surgery	
Bilateral total mastectomy (metachronous)	1
Unilateral total mastectomy	7
Unilateral partial mastectomy	5
Refused surgery	1
Pathologic type	
Solid tubular carcinoma	6
Invasive ductal carcinoma	2
Scirrhous-type carcinoma	2
Unknown	4
No extrathoracic disease	7
Metastasis to other organs	7
Local recurrence (breast)	3
Axillary lymph node	1
Liver	2
Brain	1
Bone	1
Kidney	1
Adrenal gland	1
Reason for discontinuation of systemic chemotherapy	
Progressive disease	10
Intolerance	3
Refusal	1

to systemic chemotherapy, and 1 rejected systemic chemotherapy. The median time between initial diagnosis and initial transcatheter arterial chemoembolization was 57 months (range, 17–172 months).

#### **Tumor Characteristics**

Tumor characteristics (eg, distribution, location, size) are shown in **Table 2**. Two patients had a single tumor, and 12 patients had multiple tumors. Lung and lymph node metastases were present in 8 patients, 5 patients had only lung metastasis, and 1 patient had only lymph node metastasis. Among the 13 patients who had lung tumors, 7 had bilateral tumors, and 6 had unilateral tumors. In this study, 29 tumors were assessed as target tumors. A maximum of 3 tumors were selected from each patient. Of the 29 tumors, 14 were lymph node metastases, 8 were located in the hilum, 6 were in the mediastinum, and 15 were in the lung field. The median target tumor size were 27 mm (range, 21–85 mm).

# Treatment Regimen and Selection of Embolic Material

Combinations of 2–4 anticancer drugs, which included a key drug and other drugs, were selected. Key drugs included

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