Preoperative transarterial Embolisation in bone tumors

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Abstract
Bone tumors include a variety of lesions, both primary and metastatic. The treatment modalities for bone tumors vary with the individual lesion, but in general surgical excision is the treatment of choice with other adjunctive therapies. However, surgery for many bone tumors is complex due to several factors including tumor bulk, vascularity, vicinity to vital structures and potentially inaccessible location of the lesion. Transarterial Embolisation (TAE) is one of the important adjuvant treatment modalities and in some cases it may be the primary and curative treatment. Preoperative TAE has proved to be effective in both primary and metastatic bone tumors. It reduces tumor vascularity and intraoperative blood loss, the need for blood transfusion and associated complications, allows better definition of tissue planes at surgery affording more complete excision, and hence reduced recurrence. Preoperative chemoEmbolisation has also been shown to increase the sensitivity of some tumors to subsequent chemotherapy and radiotherapy. There are several techniques and embolic agents available for this purpose, but the ultimate aim is to achieve tumor devascularization. In this review, we discuss the techniques including the choice of embolic agent, application to individual lesions and potential complications.

INTRODUCTION
The main indications for transarterial Embolisation (TAE) are to reduce preoperative and postoperative blood loss in hypervascular tumors, to simplify the excision of tumors, as a palliative measure to reduce pain, blood loss, pyrexia, and hypercalcemia associated with inoperable tumors, and in certain tumors to increase the response to chemotherapy and radiotherapy. Of these indications, most TAEs are performed as a pretreatment procedure to reduce blood loss associated with excision of many metastatic or primary hypervascular lesions. The principle behind TAE of bone tumors, as for other regions, is the precise targeting of the occlusive embolic material to tumor feeding vessels. The aim of TAE is the exclusion of the tumor capillary bed and not the major arterial feeder, as occluding only the major vessel supplying the tumor leads to revascularization of the tumor from other routes. Embolic agents are classified into liquid and particulate. The most critical factor in the choice of an occlusive agent is operator experience. In general,
particulate agents are easier to handle and require less operator experience compared to liquid agents\[6\]. The main concern in TAE is non-target Embolisation and occlusion of a non-target vessel. This can be prevented by careful review of the angiograms obtained immediately before Embolisation and meticulous care during injection of the embolic agent. In some cases, TAE may be contraindicated due to the origin of a vital artery from a tumor feeding artery, e.g., spinal artery. However, overall TAE is a safe procedure.

**TECHNIQUE**

Catheter angiography is performed prior to Embolisation to identify the tumor feeding vessels and to determine the safety of Embolisation. Particular attention should be paid when performing Embolisation in the spine to avoid the spinal arteries and in the femoral and humeral regions to avoid the vasa nervorum of the main nerves in these regions. After identification of tumor feeding arteries and the vessels to be avoided, the artery is catheterized. The choice of catheter depends on the size of the feeding vessel. However, TAE is mostly performed using a coaxial catheter system\[^4\], which comprises of a large 4-6 F catheter which is used to hook the artery and provide stability to a microcatheter (2.7 F), introduced through the larger selective catheter. Advantages of using a coaxial system include the ability to deliver embolic agent further from the parent vessel, thus reducing the risk of non-target Embolisation, easier cannulation of the hypertrophied unnamed vessels which are difficult to cannulate with the larger diagnostic catheter, preventing arterial spasm and vessel occlusion which can occur with attempted cannulation of relatively small arteries resulting in a false end point.

**Embolisation AGENTS**

The choice of embolic agent depends on the individual tumor vasculature including vessel calibre, presence of arteriovenous shunts, collateral supply to or from adjacent normal tissues and most important, operator experience\[^3\]. Embolisation agents can be classified based on whether temporary or permanent and on the basis of their physical state as liquid and particulate.

Liquid Embolisation agents include glue [N-butyl cyanoacrylate (NBCA)], absolute alcohol, Ethibloc (Ethicon, Norderstedt, Germany), sodium tetradecyl sulfate, Onyx (Microtherapeutics, Irvine, CA, USA) and particulate agents include Embosphere™ (Biosphere, France), polyvinyl alcohol (PVA)-particles (Contour™, BSIC; Cook Inc., Bloomington, IN, USA) and Gelfoam™ (Pharmacia, USA). In general, liquid embolics result in more tumor necrosis than particulate agents and are advantageous when definitive treatment is desired, but carry an increased risk of non-target Embolisation and catheter gluing, particularly in the case of tissue adhesives (cyanoacrylates) compared with particulate agents\[^7\]. As bone is a non-end organ supplied by multiple arteries, liquid agents may be associated with a greater risk of non-target Embolisation than in other tissues\[^8\]. Available evidence involving the use of liquid embolic agents in TAE of bone tumors is limited; in general, when TAE is performed to devascularize the tumor, there is little advantage over particulate embolics.

Particulate agents are relatively easy to handle. An error in particle size selection, however, may lead to venous efflux with potential for pulmonary embolism\[^7\] when smaller particles are used, or reflux when used in too large sizes or amounts or fast injections.

PVA is available in sizes ranging from 50 to 1000 μm; the commonest size used is in the 300-500 μm range. PVA has several desirable characteristics which makes it a commonly used agent. It is capable of penetrating and occluding the tumor blood supply, and it is relatively inexpensive and easy to handle. However, PVA particles can aggregate and form clumps causing catheter occlusion and some unpredictability in the level of Embolisation.

Embosphere™ (Biosphere, France) are engineered PVA particles; have a more uniform size and are compressible with easier delivery through small catheters\[^6\]. According to some authors, the 300-500 μm sized Embosphere™ particles are first choice agents\[^8\].

Gelfoam or gelatin sponge is a dissolvable sponge-like material; is considered a temporary Embolisation agent; the occluded artery usually recanalizes within a month.

Coils are usually reserved for occlusion of the distal segment of large feeding arteries, prior to superselective TAE of a tumor with particulate agent. This technique known as “backdoor Embolisation” prevents the occlusion of vessels supplying back and anterior abdominal wall muscles and also improves the efficacy of Embolisation by preventing recruitment of collaterals\[^5\]. They have a potential role in the emergency setting with an inexperienced operator or when time is lacking for other forms of Embolisation.

The basic principle in TAE is the occlusion of most of the capillary tumor bed. The occlusion of only the major tumor feeding arteries is ineffective, because of numerous collaterals in hypervascular bone tumors\[^5\].

When large intervertebral-, intercostal- or lumbar-feeding tumor arteries are targeted, backdoor Embolisation is recommended. Ideally, surgery must be performed within 3 d of Embolisation in order to avoid revascularization. Besides non-target Embolisation, a more common complication is “post-Embolisation” syndrome. This presents with pain at the target site, fever, headache and malaise. This syndrome is encountered more commonly in hepatic and renal Embolisation.

**PRIMARY BONE TUMORS**

**Aneurysmal bone cyst**

Aneurysmal bone cysts (ABCs) are highly vascular benign bone tumors. Management of ABCs depends upon their location and aggressiveness. Aggressive extremity lesions are usually treated with intralesional curettage and bone-grafting\[^5\]. Non-aggressive lesions are followed up as
they often show spontaneous regression\[9\]. Pelvic ABCs are large and their treatment is difficult because of the relative inaccessibility of the lesions, massive intraoperative bleeding related to multiple anastomoses formed.
by branches of major vessels in this region, proximity to neurovascular structures, and the potential risk to the acetabulum or sacroiliac joint. Preoperative TAE can reduce intraoperative and postoperative blood loss and in some cases embolisation can induce ossification and maturation of ABCs, avoiding surgery altogether (Figures 1 and 2). Several studies support preoperative TAE as an effective adjunct to surgery. Yildirim et al. reported two cases of pelvic ABCs treated with TAE as an adjunct to curettage and bone grafting. They performed embolisation with PVA 500-700 μm in diameter following catheterization of the main feeding artery arising from the left inferior epigastric which was followed by curettage and bone grafting. There was no evidence of recurrence at 6-mo follow-up. Embolisation of peripheral ABCs has also been reported. Börüban et al. described four cases of peripheral ABCs; in three cases, embolisation was followed by surgery and in one case of a distal femur lesion, embolisation achieved cure. As regards the embolisation agent, encouraging results have been reported with the use of NBCA. Marushima et al. reported a case of thoracic ABC treated with NBCA which was stable at 3 years following transcatheter embolisation. Rossi et al. reported their experience of using NBCA in the TAE of ABC. They performed 55 embolisations in 36 patients. The treatment was considered effective in 94% of cases with a follow-up of 2 years.

**Giant cell tumor**

Giant cell tumors (GCTs) are benign locally aggressive and highly vascularized bone tumors. The most common sites of origin are distal femur, proximal tibia and distal radius. Surgery is the treatment modality of choice for these long bone GCTs; however, local recurrence does occur. The spine is rarely involved and the most common location in the spine is the sacrum. Similar to the complexity of surgery for pelvic ABCs, sacral GCTs are difficult lesions to treat surgically. Radiotherapy is contraindicated because of its potential to induce malignant transformation. Several studies have reported embolisation as an alternative treatment method for non-resectable tumors. Börüban et al. reported a recurrent GCT lesion in the proximal fibula treated with TAE. Preoperative embolisation resulted in 80% devascularisation.
tion and surgery was performed without severe bleeding (Figures 3 and 4). Hosalkar et al.\cite{19} reported a series of nine cases treated with repeated TAE (a mean of 4.8 treatments per patient). They employed various embolic techniques and demonstrated a substantial improvement in pain scores and lack of tumor progression in seven of nine cases over a follow-up of 8.96 years. Lin et al.\cite{20} reported 18 patients with sacral GCTs managed with TAE over a 26-year period. Embolisations were performed at 2 to 4 mo intervals with the end point being the lack of a hypervascular mass. The results indicated local recurrence rates of 31% at 10 years and 43% at 15 and 20 years, respectively. GCTs may also occur in the areas of the spine other than the sacrum and studies have demonstrated the efficacy of TAE in these circumstances\cite{21}. Tsuchiya et al.\cite{22} reported a case of a GCT of the atlas which was treated with combined surgical and preoperative Embolisation of the right vertebral artery.

### Osteoblastoma

Osteoblastoma is a benign primary hypervascular tumor, most commonly originating in the spinal column. Surgical resection is the treatment of choice. However, complete resection is often complicated by extensive intraoperative bleeding. TAE reduces intraoperative bleeding, making a complete surgical resection feasible with a reduction in post-operative complications. Silva et al.\cite{23} reported successful preoperative TAE of two cases of osteoblastoma in children. Trübenbach et al.\cite{24} reported preoperative TAE in three cases of cervical osteoblastoma. Surgical resection could be performed in all cases without significant bleeding and the postoperative course was uneventful.

### Vertebral hemangioma

Vertebroplasty for vertebral hemangiomas is generally indicated for lesions without neurological deficit. When patients present with spinal pain or cord compression with neurological deficit, radiation or decompression surgery is the treatment of choice. Massive hemorrhage is often encountered during surgery from these highly vascular lesions. Several authors have shown TAE to be a useful adjunctive method to reduce perioperative blood loss (Figure 5). Jayakumar et al.\cite{25} reported 12 patients with symptomatic vertebral hemangiomas in whom particulate Embolisation was performed. Eleven of the 12 patients subsequently underwent decompressive laminectomy. On
follow-up at 8 mo, 11 patients showed improvement. Ng et al.\textsuperscript{[26]} reported a case of symptomatic thoracic vertebral hemangioma treated with preoperative TAE with NBCA.

**Osseous arteriovenous malformations**

Primary osseous arteriovenous malformations (AVMs) are rare with most lesions involving the maxilla or mandible\textsuperscript{[27]}. There are several reports of TAE or transvenous Embolisation of osseous AVMs. Katzen et al.\textsuperscript{[28]} reported TAE of an AVM of the tibia with remission of symptoms at 1 year of follow-up.

**Osteosarcoma**

Surgery along with adjunctive systemic chemotherapy is the standard treatment for osteosarcomas; however, transarterial chemoEmbolisation in combination with limb salvage surgery has been shown to yield encouraging results (Figure 6). Chu et al.\textsuperscript{[29]} reported their experience with transarterial chemolEmbolisation in 32 patients with osteosarcomas who subsequently underwent limb salvage surgery. They employed a triple-drug regimen; following infusion of the chemotherapeutic agents, the vessels were embolized with a variety of embolic agents. They demonstrated a reduced incidence of local recurrence, TAE without chemotherapy has also been shown to be effective as an adjunct to surgery\textsuperscript{[30,31]}.

**Other primary bone lesions**

Isolated case reports of TAE in other rare bone pathologies have been reported. Findlik et al.\textsuperscript{[32]} reported preoperative TAE of a rib hemangiopericytoma. Sanchez-Mejia et al.\textsuperscript{[33]} reported a case of sacral epithelioid angiosarcoma treated with TAE.

**Bone metastases**

There are several indications for TAE in bone metastases: preoperative TAE to reduce vascularity and intraoperative blood loss; palliation of bone pain, fever, hypercalcemia and other rheological features; to enhance sensitivity to chemotherapy or radiotherapy. The aim is to improve patient quality of life. Barton et al.\textsuperscript{[34]} in their review of the literature found that the most common indication for Embolisation in bone tumors is bone metastases from thyroid (Figure 7) and renal carcinoma (RCC) (Figure 8) which are hypervascular in 65%-70% of cases. Forauer et al.\textsuperscript{[35]} reported a retrospective review of 21 patients presenting for palliative Embolisation of painful RCC skeletal metastases. Thirty separate Embolisations were performed and it was concluded that Embolisation can provide effective palliation in patients with renal skeletal metastases who otherwise have therapeutic options. Van Tol et al.\textsuperscript{[36]} reported a significant initial reduction in serum thyroglobulin levels suggesting reduction of tumor bulk in five patients with large thyroid carcinoma skeletal metastases in whom they performed TAE in combination with radioiodine therapy. Guzman et al.\textsuperscript{[37]} reported preoperative TAE in 24 patients with hypervascular vertebral metastases. They concluded that the procedure is safe and facilitates surgical excision. Sun et al.\textsuperscript{[38]} reported the effectiveness of preoperative Embolisation to reduce blood loss during surgical repair of bone metastases from RCC. They recruited 16 patients with bone metastases for preoperative Embolisation and concluded that preoperative TAE reduced intraoperative blood loss with no adverse effects on healing. Few studies have demonstrated the effectiveness of TAE in hepatocellular carcinoma (HCC) bone metastases. Hansch et al.\textsuperscript{[39]} reported a case of TAE of an unusual HCC to the humerus. Uemura et al.\textsuperscript{[40]} compared the relative efficacy of TAE, TAE with external radiotherapy and external radiotherapy alone in 39 metastatic bone lesions from HCC. They concluded that TAE alone provides immediate pain relief, whereas a combination of TAE and external radiotherapy is required for permanent pain relief.

**REFERENCES**

1. Börüban S, Sancak T, Yıldız Y, Sağlık Y. Embolisation of benign and malignant bone and soft tissue tumors of the extremities. Diag Interv Radiol 2007; 13: 164-171.

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**Figure 8** Preoperative Embolisation in a metastatic lesion from renal cell carcinoma in an elderly male. A: Fifty-two-year-old male with renal cell carcinoma (RCC) and a large destructive lesion of the right femoral metaphysis extending to involve the proximal diaphysis. Preoperative Embolisation was planned to reduce tumour vascularity. Metastases from thyroid carcinoma and RCC are highly vascular; B and C: Right common femoral angiogram revealed marked tumor vascularity; D: Delayed phase image shows profound tumor vascularity; E: Embolisation was performed with 300-500 μm polyvinyl alcohol particles and marked reduction (90%) in tumour vascularity was achieved.
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1. **Kauffmann G**, Wimmer B, Bischoff W, Adler C, Strecer EP. [Fundamental experiments for therapeutic artery occlusion by angiography catheters (author’s transl)]. *Radiologie* 1977; 17: 489-491

2. **Radeleff B**, Eiers M, Lopez-Benitez R, Noedelge H, Hallscleit P, Grenacher L, Libicher M, Zeifang F, Meeder PJ, Kauffmann GW, Richter GM. Transarterial Embolisation of primary and secondary tumors of the skeletal system. *Eur J Radiol* 2006; 58: 68-75

3. **Brado M**, Hansmann HJ, Richter GM, Kauffmann GW. [Interventional therapy of primary and secondary tumors of the spine]. *Orthopade* 1998; 27: 269-273

4. **Munk PL**, Legenheim GM. Musculoskeletal intervention radiology: applications to oncology. *Semin Roentgenol* 2007; 42: 164-179

5. **Owen RJ**. Embolisation of musculoskeletal bone tumors. *Semin Intervent Radiol* 2010; 27: 111-123

6. **Brown KT**. Fatal pulmonary complications after arterial Embolisation with 40-120- micro m tris-acryl gelatin microspheres. *J Vasc Interv Radiol* 2004; 15: 197-200

7. **Pagapelopoulos PJ**, Choudhury SN, Frassica FJ, Bond JR, Unni KK, Sim FH. Treatment of aneurysmal bone cysts of the pelvis and sacrum. *J Bone Joint Surg Am* 2001; 83-A: 1674-1681

8. **Malghem J**, Malldague B, Esselinckx W, Noel H, De Nayer P, Vincent A. Spontaneous healing of aneurysmal bone cysts. A report of three cases. *J Bone Joint Surg Br* 1989; 71: 645-650

9. **Mucco RC**, Sheft D5, Takedo S, Healey JH. The treatment of aneurysmal bone cyst. *Clin Orthop Relat Res* 1995; 315: 157-163

10. **Murphy WA**, Strecer EB, Schoenecker PL. Transcatheter Embolisation therapy of an ischial aneurysmal bone cyst. *J Bone Joint Surg Br* 1982; 64: 166-168

11. **Yildirim E**, Ersozli S, Kirbas I, Ozturk AF, Akkaya T, Karadeli E. Treatment of pelvic aneurysmal bone cysts in two children: selective arterial Embolisation as an adjunct to curettage and bone grafting. *Diagn Interv Radiol* 2007; 13: 49-52

12. **Marushima A**, Matsumura Y, Suzuki K, Takigawa T, Kujirakaya O, Anno H, Matsumura A. Selective arterial Embolisation with n-butyl cyanoacrylate in the treatment of aneurysmal bone cyst of the thoracic vertebra: a case report. *Spine* (Phila Pa 1976) 2009; 34: E230-E234

13. **Rossi G**, Rimondi E, Bartalena T, Gerardi A, Alberghini M, Staals EL, Errani C, Bianchi G, Toscano A, Mercuari M, Vanel M. Selective arterial Embolisation of 36 aneurysmal bone cysts of the skeleton with N-2-butyl cyanoacrylate. *Skeletal Radiol* 2010; 39: 161-167

14. **Lin PP**, Guzel VB, Moura MF, Wallace S, Benjamin RS, Weber KL, Morello FA, Gokaslan ZL, Yasko AW. Long-term follow-up of patients with giant cell tumor of the sacrum treated with selective arterial Embolisation. *Cancer* 2002; 95: 1317-1325

15. **Lackman RD**, Khoury LD, Esmail A, Donthineni-Rao R. The treatment of sacral giant-cell tumours by serial arterial Embolisation. *J Bone Joint Surg Br* 2002; 84: 873-877

16. **Broadaus WC**, Grady MS, Delashaw JB, Ferguson RD, Jane JA. Preoperative selective arteriolar Embolisation: a new approach to enhance resectability of spinal tumors. *Neurosurgery* 1999; 37: 755-759

17. **Bigiani R**, De Cristofaro R, Ruggieri P, Boriani S. Giant-cell tumor of the spine. A case report. *J Bone Joint Surg Am* 1990; 72: 1102-1107

18. **Hosalkar HS**, Jones KJ, King JJ, Lackman RD. Serial arterial Embolisation for large sacral giant-cell tumors: mid- to long-term results. *Spine* (Phila Pa 1976) 2007; 32: 1107-1115

19. **Lin PP**, Guzel VB, Moura MF, Wallace S, Benjamin RS, Weber KL, Morello FA, Gokaslan ZL, Yasko AW. Long-term follow-up of patients with giant cell tumor of the sacrum treated with selective arterial Embolisation. *Cancer* 2002; 95: 1317-1325

20. **Luther N**, Bilsky MH, Härtl R. Giant cell tumor of the spine. *Neurosurg Clin N Am* 2008; 19: 49-55

21. **Tsuchiya H**, Kubo Y, Sakurada K, Sonoda Y, Saito S, Kayama T. [A case of giant cell tumor in atlas]. *No Shinkei Geka* 2005; 38: 817-825

22. **Silva ML**, Bruntyelle F. Embolisation of vascular lesions of the spinal column in childhood: a report of three cases. *Neuroradiology* 1996; 38: 809-811

23. **Trübenbach J**, Nägele T, Bauer T, Ernemann U. Preoperative Embolisation of cervical spine osteoblastomas: report of three cases. *AJNR Am J Neuroradiol* 2006; 27: 1910-1912

24. **Jayakumar PN**, Vasudev MK, Srikanth SG. Symptomatic vertebroplasty: endovascular treatment of 12 patients. *Sporial Cord* 1997; 35: 624-628

25. **Ng WV**, Clifton A, Moore AJ, Preoperative endovascular Embolisation of a vertebral haemangioma. *J Bone Joint Surg Br* 1997; 79: 808-811

26. **Kelly DE**, Terry BC, Small EW. Arteriovenous malformation of the mandible: report of case. *J Oral Surg* 1977; 35: 387-393

27. **Katzen BT**, Said S. Arteriovenous malformation of bone: an experience with therapeutic Embolisation. *ARJR Am J Roentgenol* 1981; 136: 427-429

28. **Chu JP**, Chen W, Li JP, Zhuang WQ, Huang YH, Huang ZM, Yang YJ. Clinicopathological features and results of transcatheter arterial chemoEmbolisation for osteosarcoma. *Cardiovasc Intervent Radiol* 2007; 30: 201-206

29. **Crews KR**, Liu T, Rodriguez-Calindo C, Tan M, Meyer WH, Panetta JC, Link MP, Dow NC. High-dose methotrexate pharmacokinetics and outcome of children and young adults with osteosarcoma. *Cancer* 2004; 100: 1724-1733

30. **Wang MQ**, Dake MD, Wang ZP, Cui ZP, Gao YA. Isolated lower extremity chemotherapeutic infusion for treatment of osteosarcoma: experimental study and preliminary clinical report. *J Vasc Interv Radiol* 2001; 12: 731-737

31. **Finkl S**, Akan H, Bars S, Atici AG, Uzun O, Erkan L. Preoperative Embolisation in surgical treatment of a primary hemangiopericytoma of the rib: a case report. *J Korean Med Sci* 2005; 20: 316-318

32. **Sanchez-Mejia RO**, Ojemark G, Simko J, Chaudhary UB, Levy J, Lawton MT. Sacral epithelioid angiosarcoma associated with a bleeding diathesis and spinal epidural hematoma: case report. *J Neurosurg Spine* 2006; 4: 246-250

33. **Barton PP**, Wanneck RE, Karmel JF, Rischtj P, Kramer J, Lechner GL. Embolisation of bone metastases. *J Vasc Interv Radiol* 1996; 7: 81-88

34. **Forauer AR**, Kent E, Cwikiel W, Esper P, Redman B. Selective palliative transcatheter Embolisation of bony metastases from renal cell carcinoma. *Acta Oncol* 2007; 46: 1012-1018

35. **Van Tol KM**, How JM, Jager PL, Vermeij A, Dullaart RP, Links TP. Embolisation in combination with radioiodine therapy for bone metastases from differentiated thyroid carcinoma. *Clin Endocrinol (Oxf)* 2000; 52: 653-659

36. **Guzman R**, Dubach-Schwizer S, Heini P, Lovblad KO, Kalmannen D, Schrott G, Remonda L. Preoperative transcatheter Embolisation of vertebral metastases. *Eur Spine J* 2005; 14: 263-268

37. **Sun S**, Lang EV. Bone metastases from renal cell carcinoma: preoperative Embolisation. *J Vasc Interv Radiol* 1998; 9: 263-269

38. **Hansch A**, Neumann R, Pfeil A, Marintchev I, Pfeiderer S, Gajda M, Kaiser WA. Embolisation of an unusual metastatic site of hepatocellular carcinoma in the humerus. *World J Gastroenterol* 2009; 15: 2280-2282

39. **Uemura A**, Fujita H, Yasaoka H, Yasaoka S, Osaka I, Goto N, Shinozaki M, Ito H. Transcatheter arterial Embolisation for bone metastases from hepatocellular carcinoma. *Eur Radiol* 2001; 11: 1457-1462