INTRODUCTION:
It is known that metastatic bone lesions often represent osteolytic changes, which reduce bone strength and eventually lead to fractures. When a cancer patient is found to have a metastatic bone lesion, physicians should properly estimate the risk of pathological fracture. The increasing number of cancer patients and elongation of survival periods by multimodality therapy may increase the importance of the estimation of the risk for the pathological fractures.

The goal of the current study was to clarify the relationship between the location or the size of osteolytic lesion and the reduction of strength of the femur using CT based 3-dimensional finite element (CT/FE) method. Particularly, we focused on the torsional strength of the femur with osteolytic lesions in the current study.

SUBJECTS and METHODS:
CT data of the right femur from two volunteers including a healthy 33-year-old male patient (177 cm, 78 kg) without any histories of bone disease and a 71-year-old female patient (146 cm, 48 kg) with primary osteoporosis were examined to develop FE models in the present study. Bone mineral density (BMD) was determined for each of them using dual-energy X-ray absorptiometry. Data were collected after permission from the local ethics committee.

Development and analysis of the 3D- FE femur model:
Three-dimensional FE models were developed from the CT data using the software, MECHANICAL FINDER. Bone was modeled using 3-mm tetrahedron elements. The outer surface of the cortical bone was modeled using three nodal-point shell elements with a thickness of 0.3 mm. The mechanical properties of each element were computed from the Hounsfield unit values in the cortical bone.

Simulation of the osteolytic lesion:
To simulate the presence of osteolytic bone tumors, we created a spherical defect at the level of the isthmus of the femoral shaft. The diameter of the defects and the distance from the center of femur, were changed in a stepwise manner. The diameters were 5, 10, 15, 20, 21, 22, 23, 24, 25 and 30 mm in a healthy adult male subject, and 5, 10, 15, 20, 21, 22, 23, 24, 25 and 26 mm in an osteoporotic female subject. The distance between the center of the spherical defect and the femoral shaft was increased by 2 mm in the ventral direction on the axial plane.

In the axial plane at the center of the spherical defect, the shape of the bony defect was classified into three types; inner erosion, cortical disruption, and outer erosion (Fig.1). The percentage of the cortical bone loss in the cross-sectional area was measured with the Image J software. The defect rate of the cortex was calculated as the area of cortical defects divided by the area of the original cortex.

Virtual Mechanical testing:
To mimic the twisting of the legs, two virtual box-type fixtures (10 × 10 × 5 cm) were designed to hold the proximal and distal part of the femurs. The proximal fixture was fixed completely on the lesser trochanter. The central axis of the fixture was aligned with the long axis of the femoral shaft. Torsional forces were symmetrically applied on the diagonal corners in the axial planes of the proximal fixture (Fig.2). The distal fixture was placed on the femoral condyle to restrain the model. The virtual loads were applied to the proximal fixture until fracture occurred, using incremental increases of 49 N-m (5 kgf-m).

Data analyses:
To determine the relationship between the failure load and the defect rate of the cortex in each defect type, Pearson’s product moment correlation coefficient (r) was calculated using the software, Graph Pad Prism (version 5.0a).

RESULTS:
The BMD of the right femoral neck was 0.953 g/cm² (T-score: 1.83) in the healthy male subject, and was 0.608 g/cm² (T-score: -3.18) in the osteoporotic female subject, respectively. The site of the fracture was the lateral edge of the cortical defect.

In healthy male subject, the correlation coefficients between the defect rate and the failure load in the cortical disruption type, the inner erosion type and the outer erosion type were \( r = -0.8744 \) (n=82, 95% confidence interval: -0.9173 to -0.8113, p < 0.0001), \( r = 0.9001 \) (n=21, 95% confidence interval: -0.9591 to -0.7660, p < 0.0001) and \( r = -0.8907 \) (n=31, 95% confidence interval: -0.9464 to -0.7836, p < 0.0001), respectively.

In osteoporotic female subject, the correlation coefficients between the defect rate and the failure load in the cortical disruption type, the inner erosion type and outer erosion type were \( r = -0.9199 \) (n=59, 95% confidence interval: -0.9518 to -0.8683, p < 0.0001), \( r = 0.5098 \) (n=18, 95% confidence interval: -0.7889 to -0.05617, p < 0.05), and \( r = -0.3836 \) (n=15, 95% confidence interval: -0.9441 to -0.5669, p < 0.0001), respectively (Fig.3).

DISCUSSION AND CONCLUSION:
Our CT-based FE models of the femur with a simulated bony defect clearly demonstrated that there was a negative correlation between the defect rate of the cortex and the failure load in the types of cortical disruption and inner erosion. These trends were mutual both in the normal and in the osteoporotic bones. Bone strength had a greater reduction with perforation of the cortex and was dependent on the defect rate of the cortex both with and without perforation of the cortex.

We believe that these results can be utilized for the risk assessment of pathological fractures due to osteolytic lesions, especially in the condition of twisting of the patient’s leg.