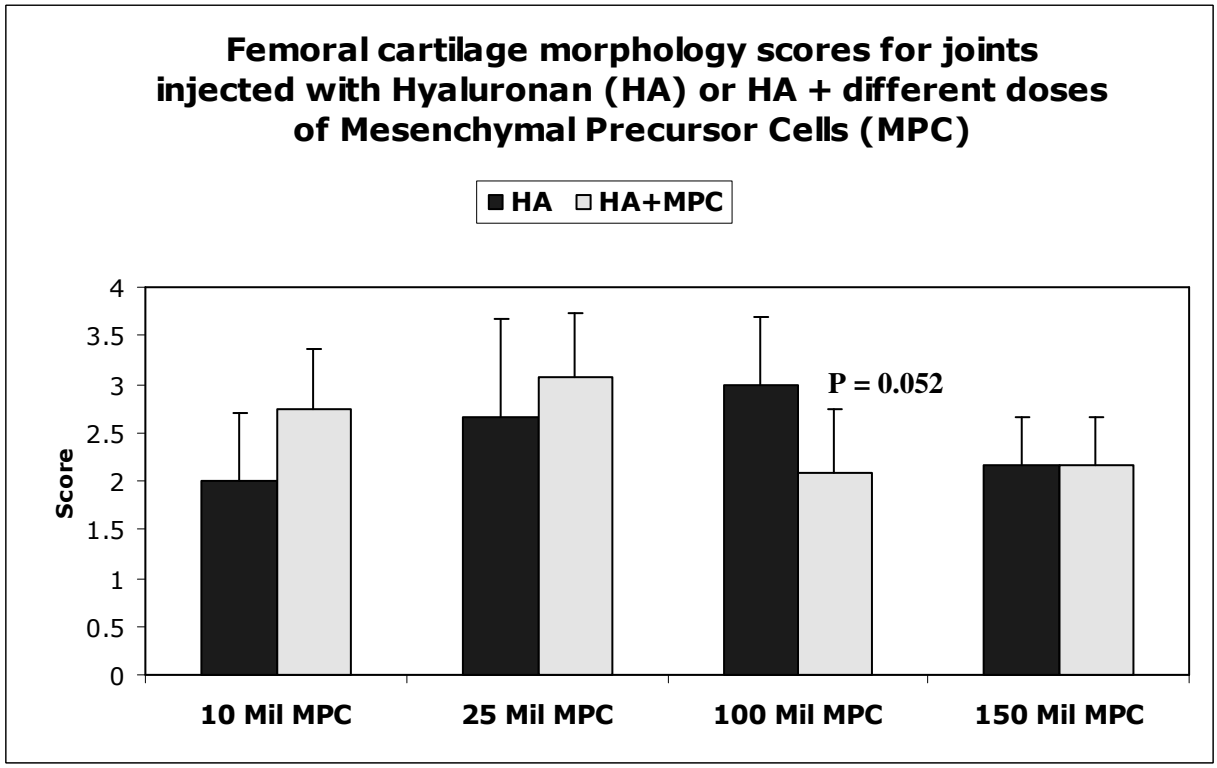

Femoral cartilage morphology scores for joints injected with Hyaluronan (HA) or HA + different doses of Mesenchymal Precursor Cells (MPC)
HA
HA+MPC
Score
4
3.5
3
2.5
2
1.5
1
0.5
0
P = 0.052
10 Mil MPC
25 Mil MPC
100 Mil MPC
150 Mil MPC

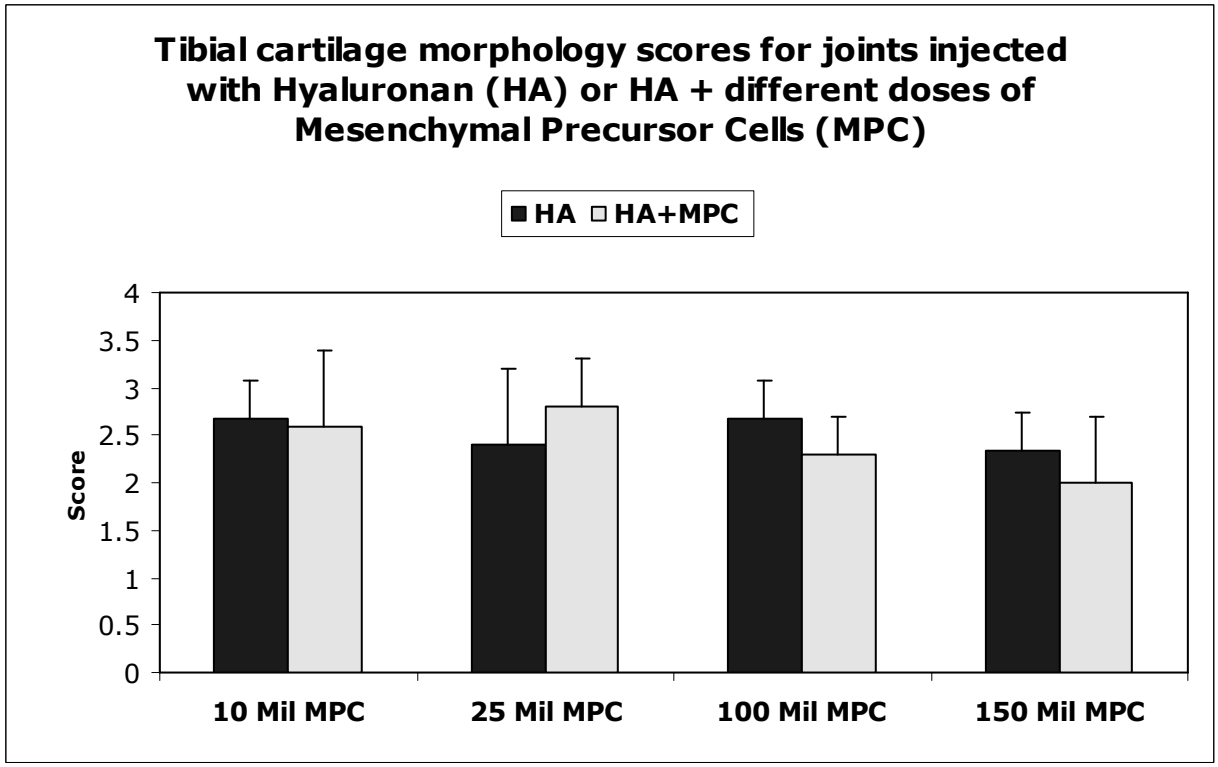

Tibial cartilage morphology scores for joints injected with Hyaluronan (HA) or HA + different doses of Mesenchymal Precursor Cells (MPC)
HA
HA+MPC
Score
4
3.5
3
2.5
2
1.5
1
0.5
0
10 Mil MPC
25 Mil MPC
100 Mil MPC
150 Mil MPC

Figure 1

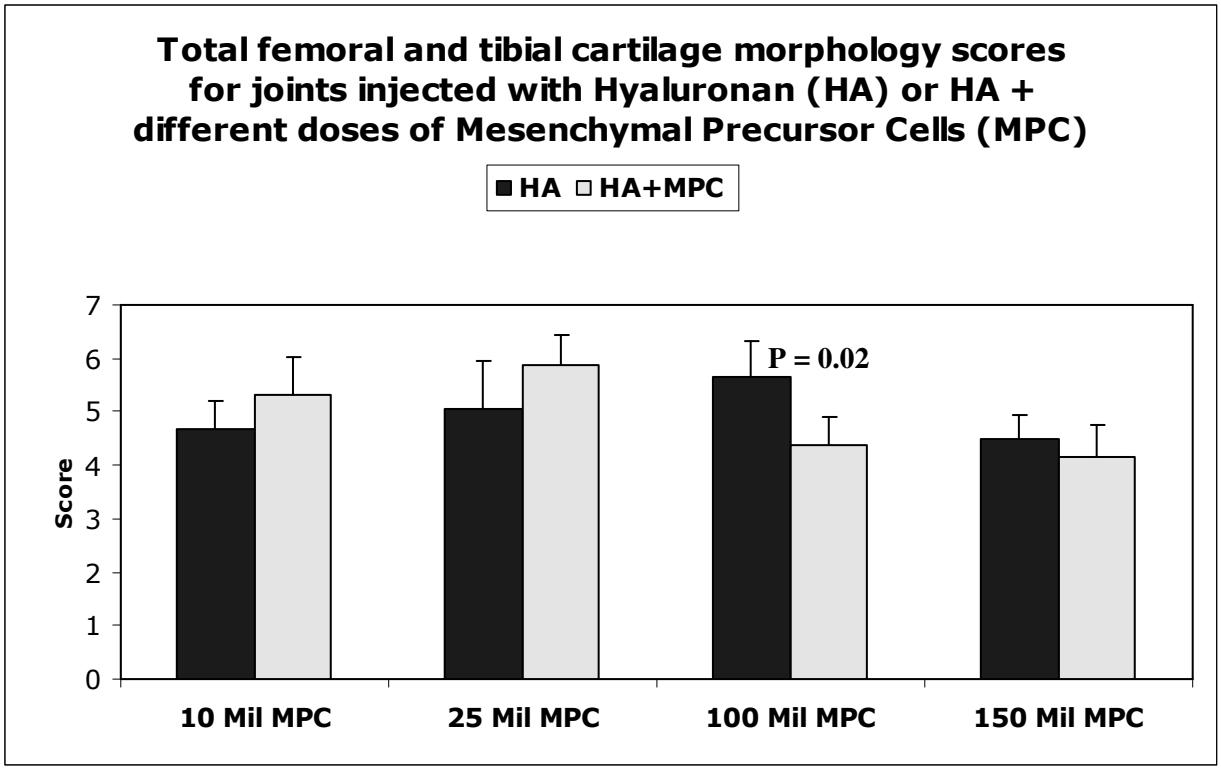
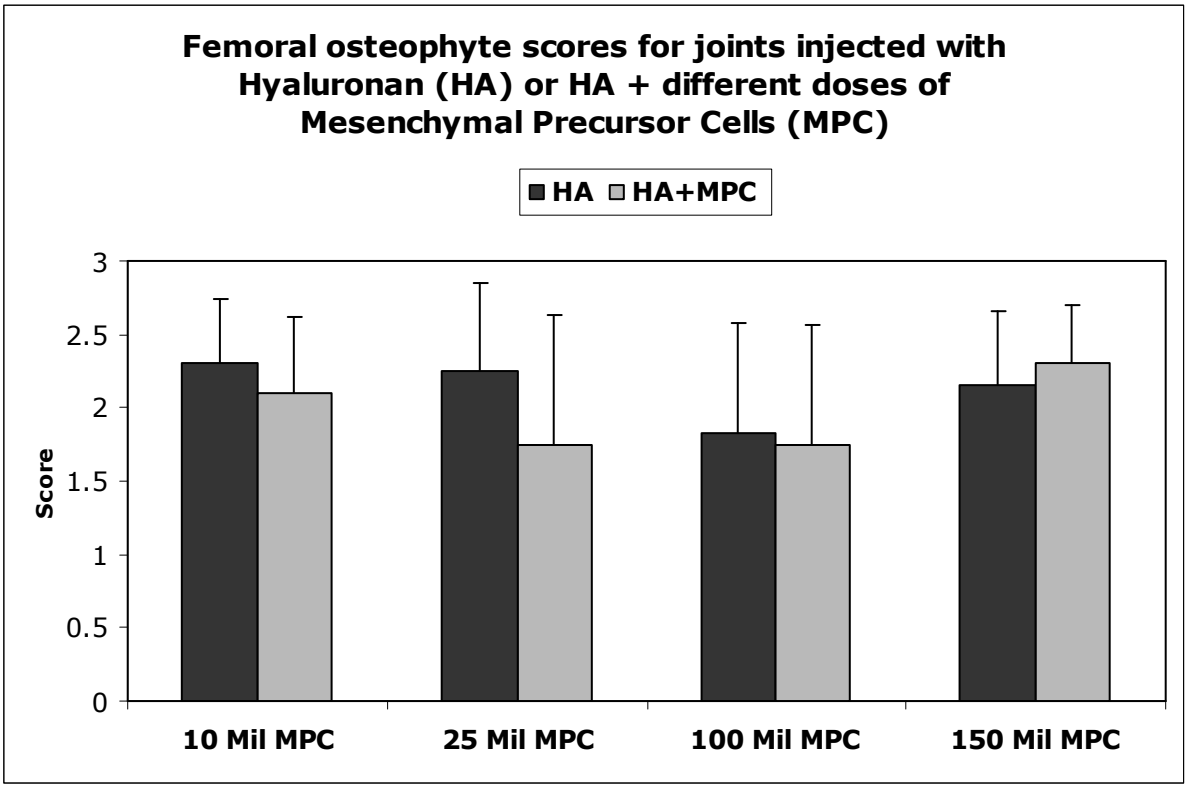


Figure 1 (continued)


Femoral osteophyte scores for joints injected with Hyaluronan (HA) or HA + different doses of Mesenchymal Precursor Cells (MPC)
HA
HA+MPC
Score
3
2.5
2
1.5
1
0.5
0
10 Mil MPC
25 Mil MPC
100 Mil MPC
150 Mil MPC

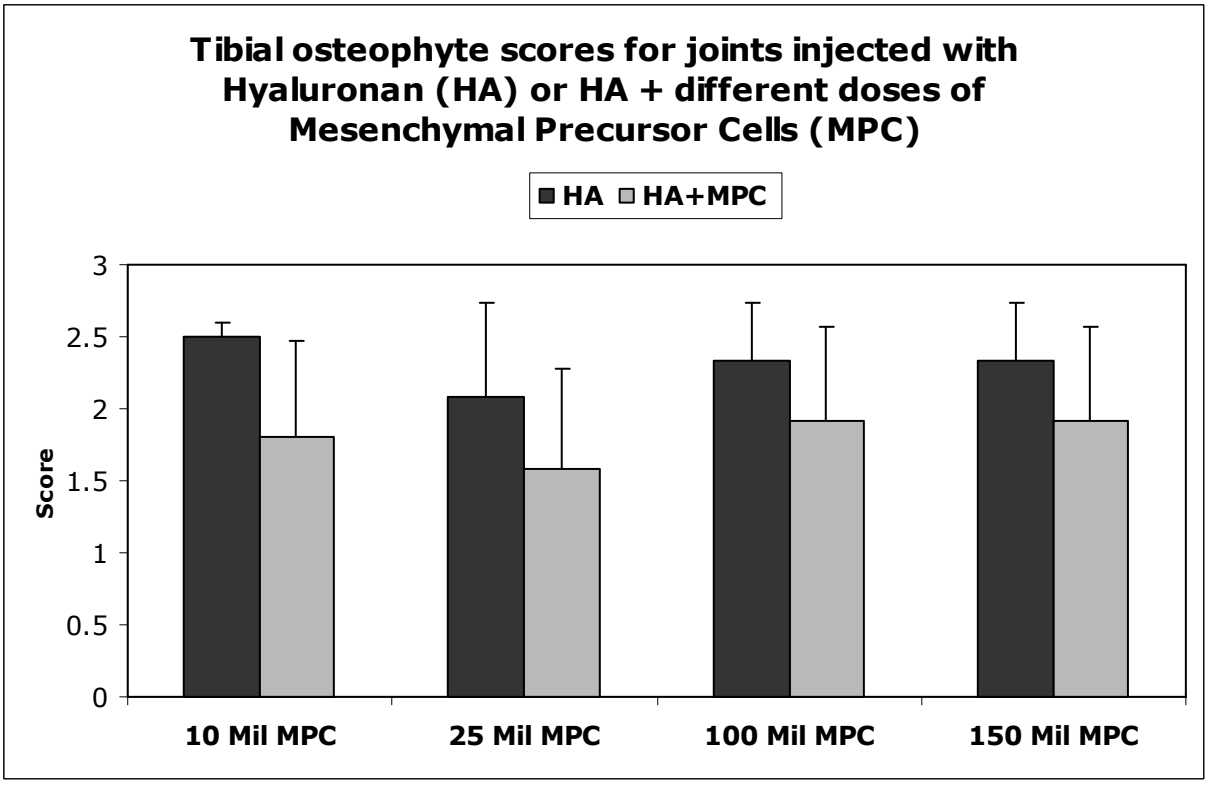

Tibial osteophyte scores for joints injected with Hyaluronan (HA) or HA + different doses of Mesenchymal Precursor Cells (MPC)
HA
HA+MPC
Score
3
2.5
2
1.5
1
0.5
0
10 Mil MPC
25 Mil MPC
100 Mil MPC
150 Mil MPC

Figure 2

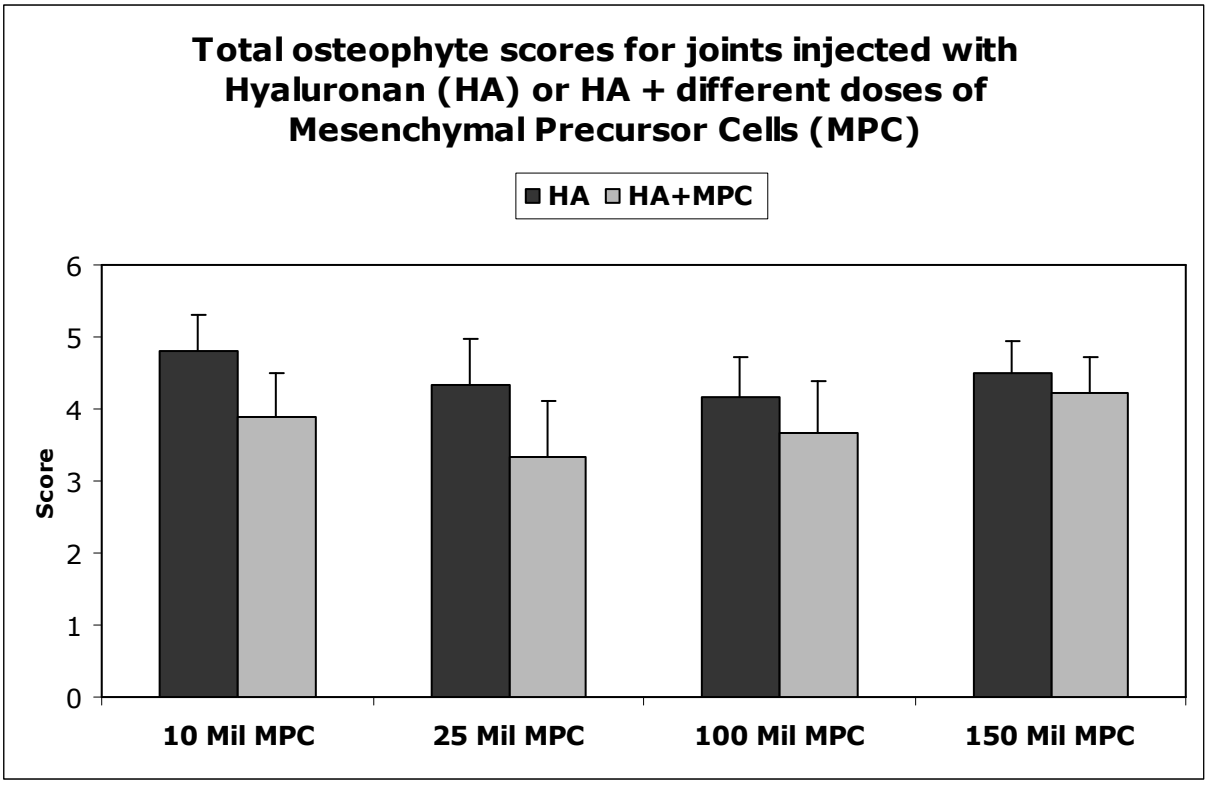


Figure 2 (continued)

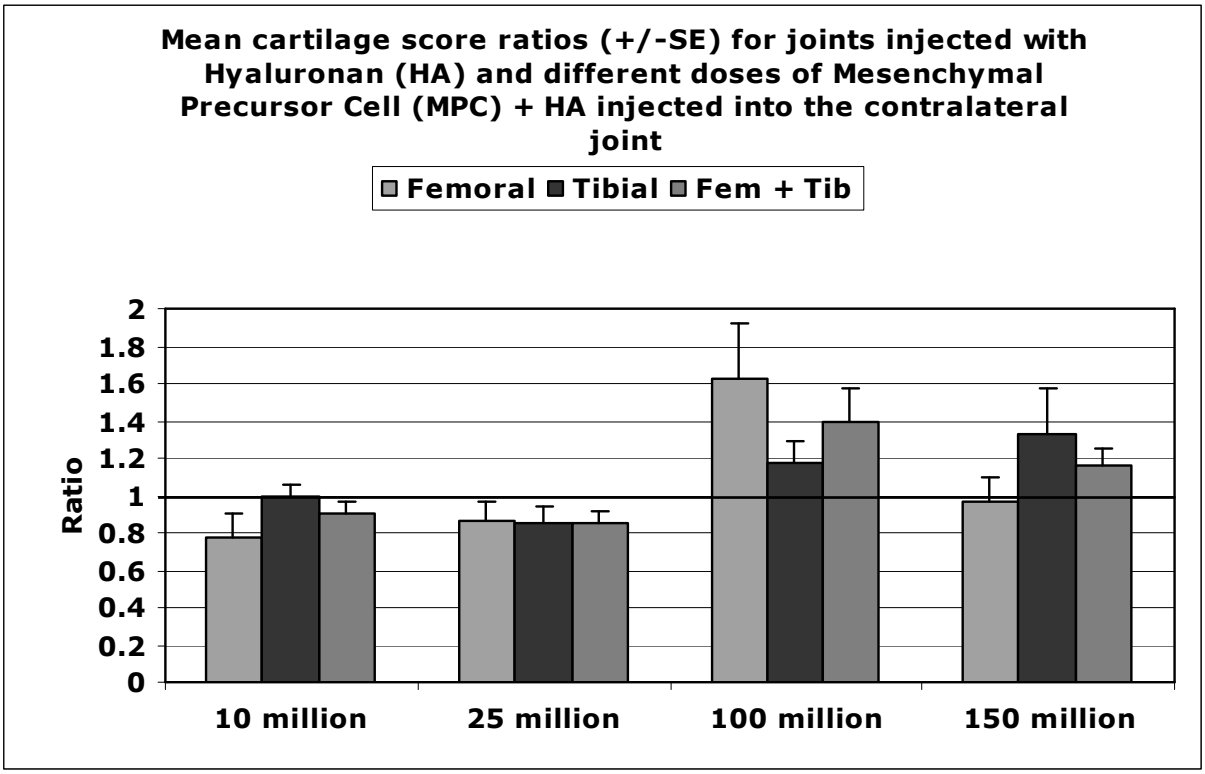

Mean cartilage score ratios (+/-SE) for joints injected with Hyaluronan (HA) and different doses of Mesenchymal Precursor Cell (MPC) + HA injected into the contralateral joint
Femoral
Tibial
Fem + Tib
Ratio
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
10 million
25 million
100 million
150 million

Figure 3

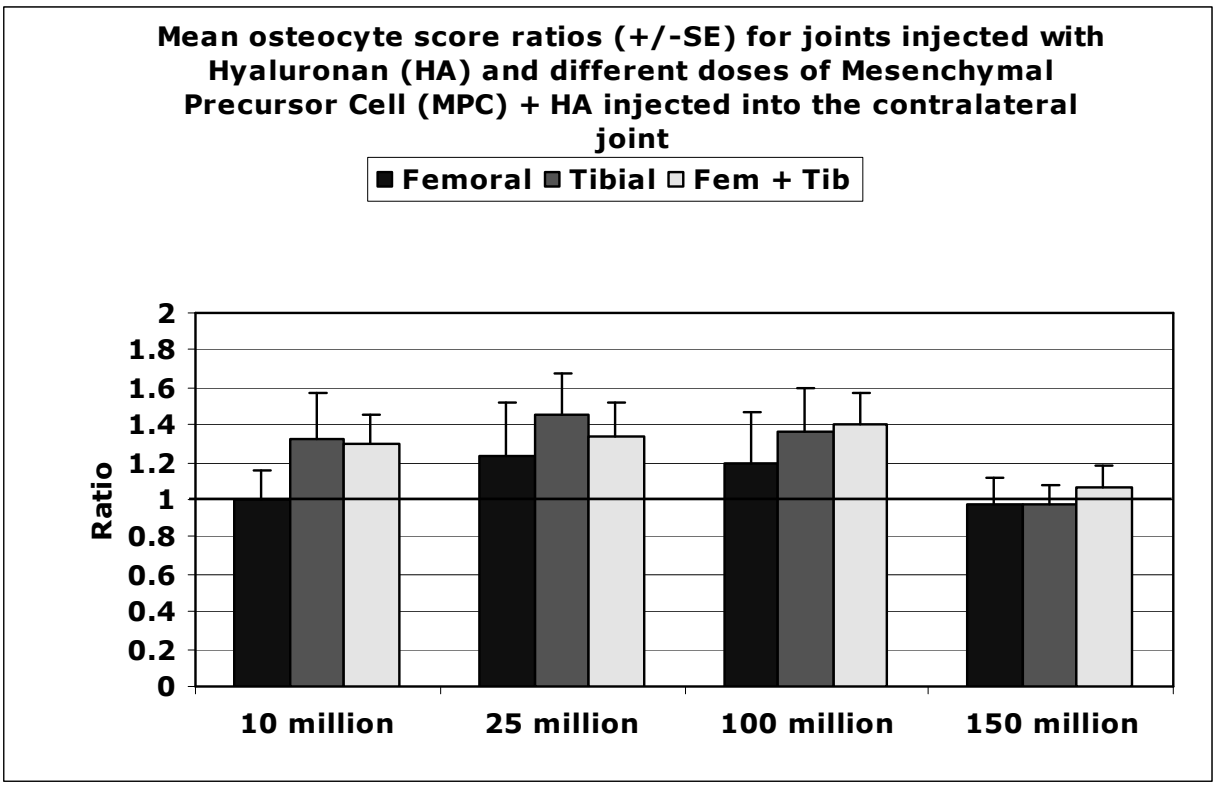

Mean osteocyte score ratios (+/-SE) for joints injected with Hyaluronan (HA) and different doses of Mesenchymal Precursor Cell (MPC) + HA injected into the contralateral joint
Femoral
Tibial
Fem + Tib
Ratio
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
10 million
25 million
100 million
150 million

Figure 4

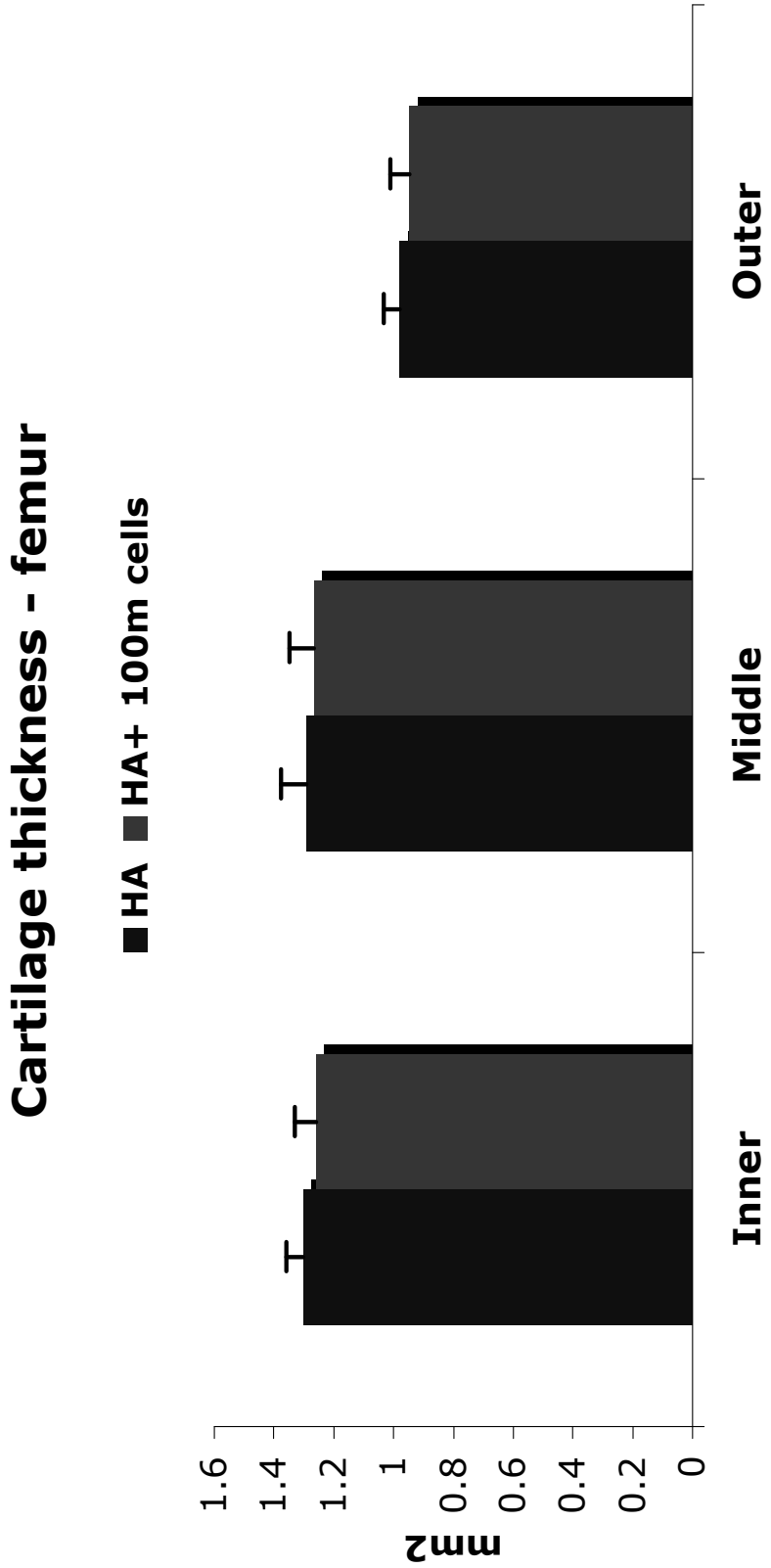

Cartilage thickness - femur
HA
HA+ 100m cells
mm2
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
Inner
Middle
Outer

Figure 5

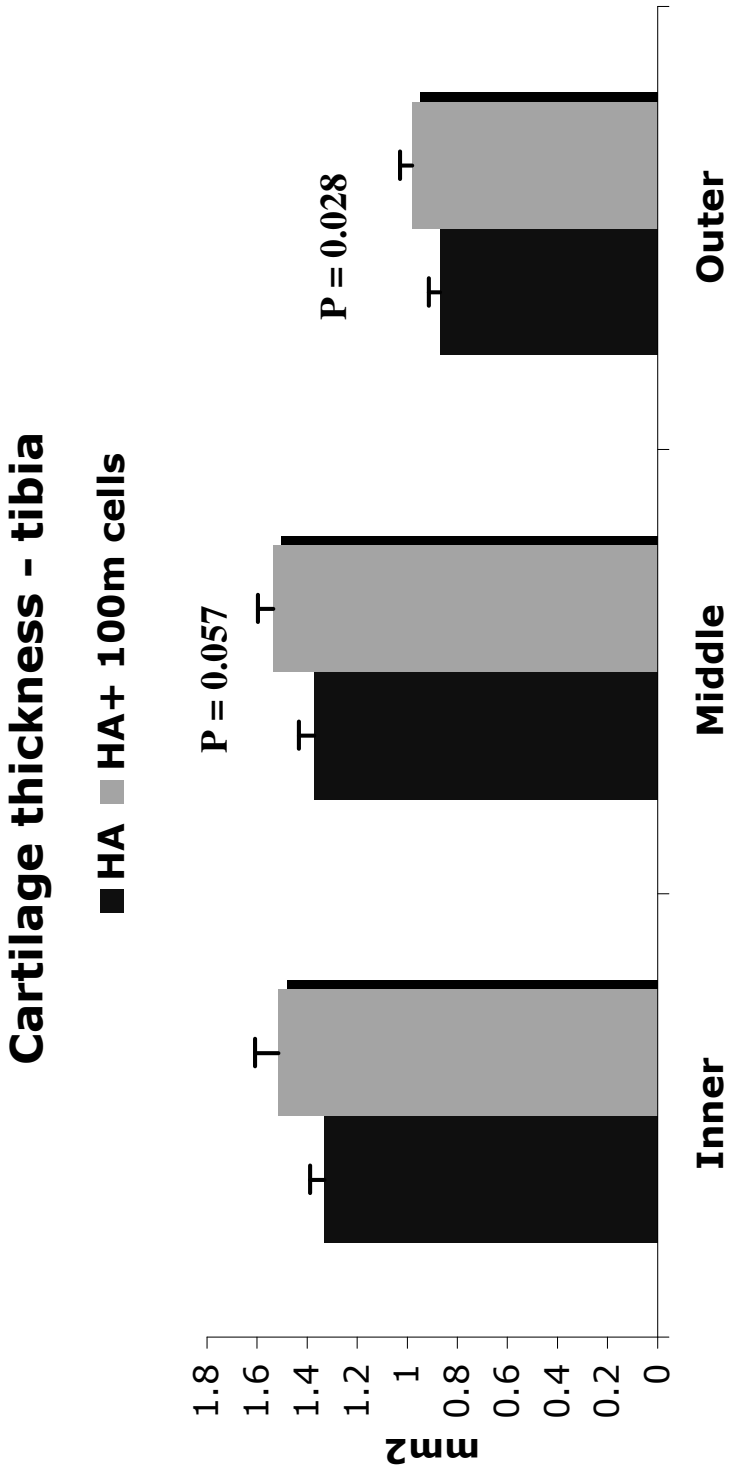


Figure 5 (continued)

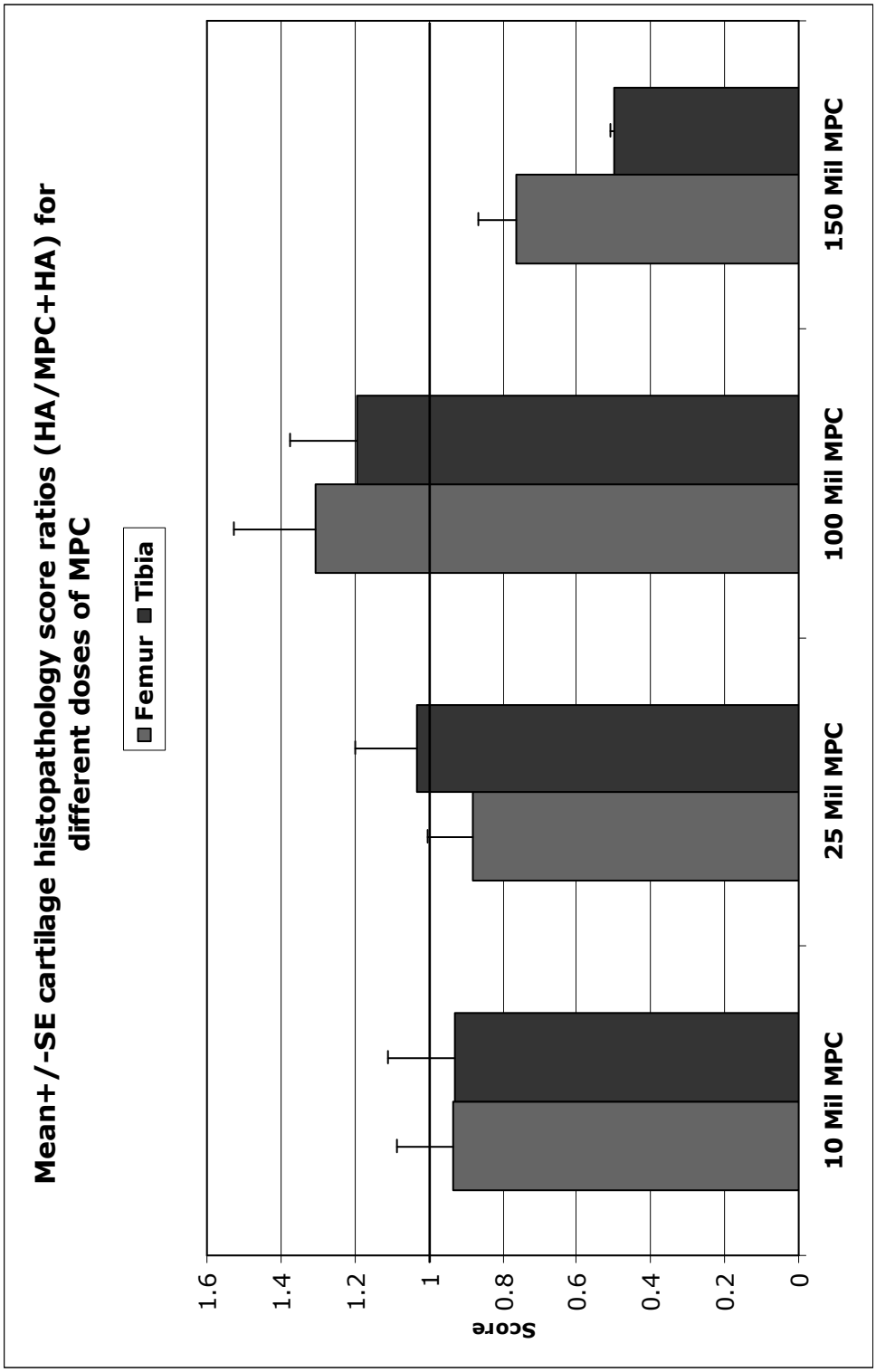
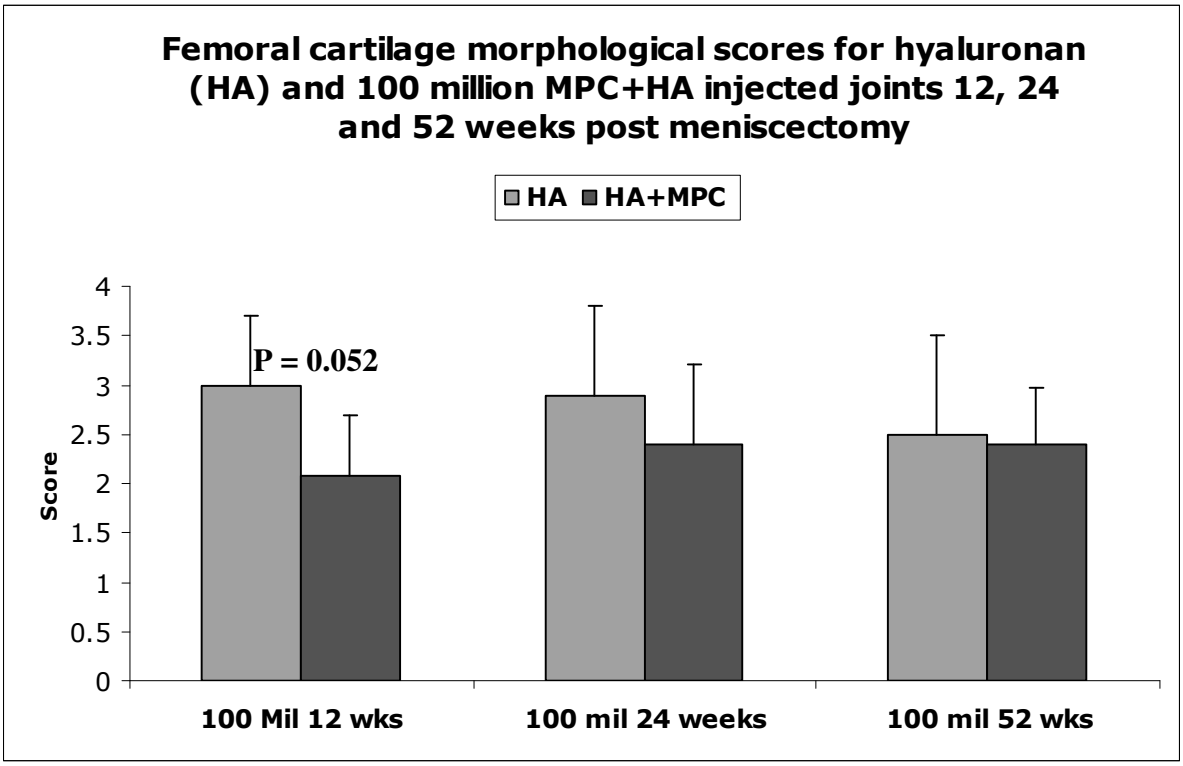

Mean+/-SE cartilage histopathology score ratios (HA/MPC+HA) for different doses of MPC
Femur
Tibia
Score
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
10 Mil MPC
25 Mil MPC
100 Mil MPC
150 Mil MPC

Figure 6


Femoral cartilage morphological scores for hyaluronan (HA) and 100 million MPC+HA injected joints 12, 24 and 52 weeks post meniscectomy
HA
HA+MPC
Score
4
3.5
3
2.5
2
1.5
1
0.5
0
P = 0.052
100 Mil 12 wks
100 mil 24 weeks
100 mil 52 wks

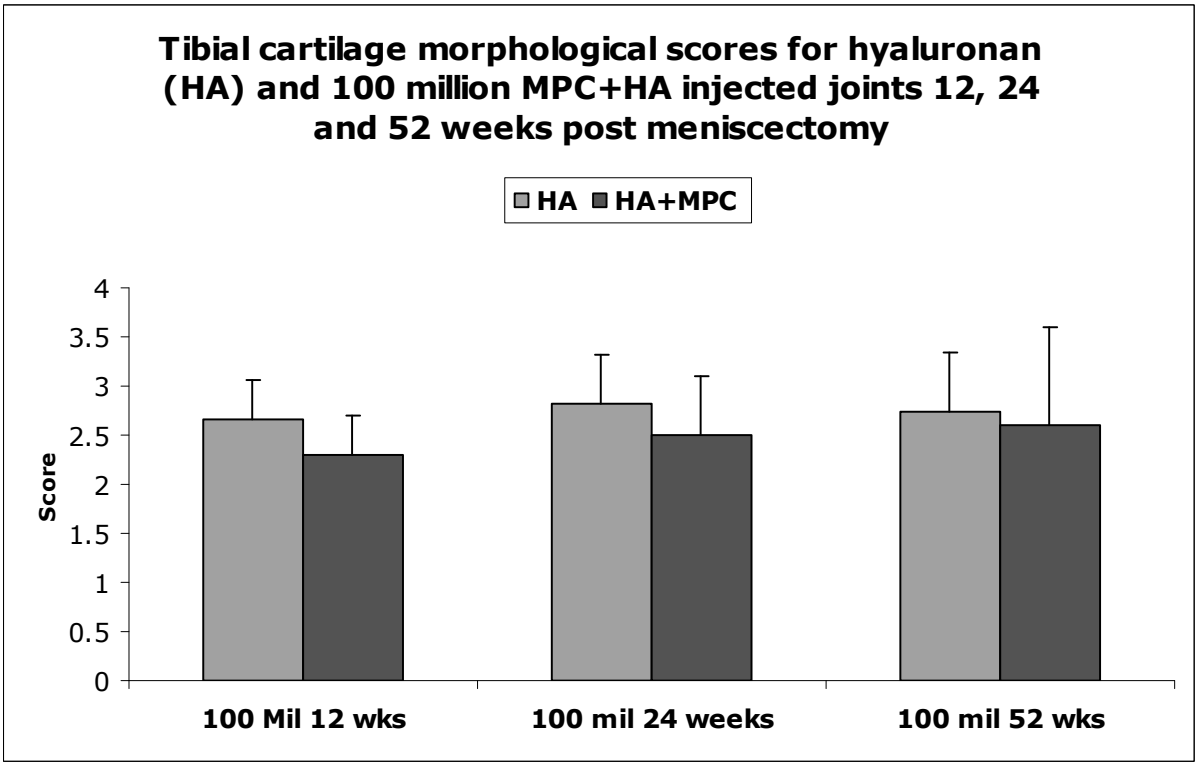

Tibial cartilage morphological scores for hyaluronan (HA) and 100 million MPC+HA injected joints 12, 24 and 52 weeks post meniscectomy
HA
HA+MPC
Score
4
3.5
3
2.5
2
1.5
1
0.5
0
100 Mil 12 wks
100 mil 24 weeks
100 mil 52 wks

Figure 7

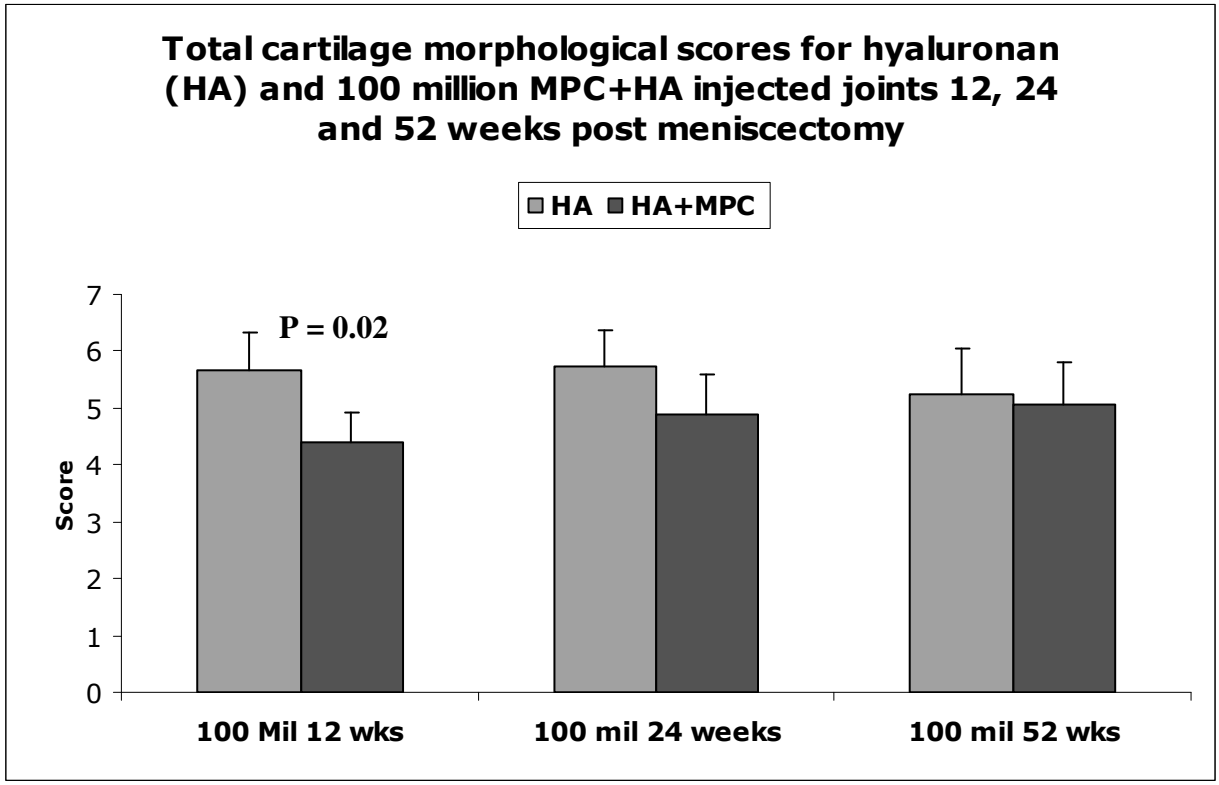
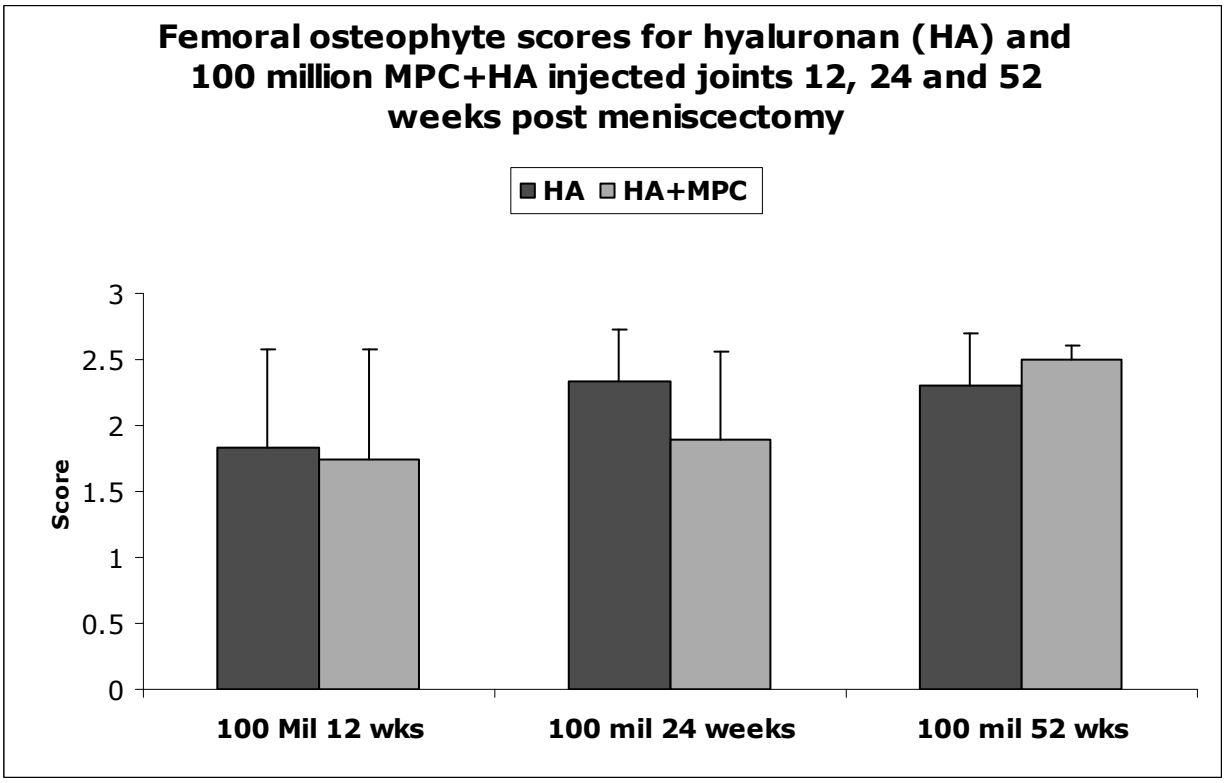


Figure 7 (continued)


Femoral osteophyte scores for hyaluronan (HA) and 100 million MPC+HA injected joints 12, 24 and 52 weeks post meniscectomy
HA
HA+MPC
Score
3
2.5
2
1.5
1
0.5
0
100 Mil 12 wks
100 mil 24 weeks
100 mil 52 wks

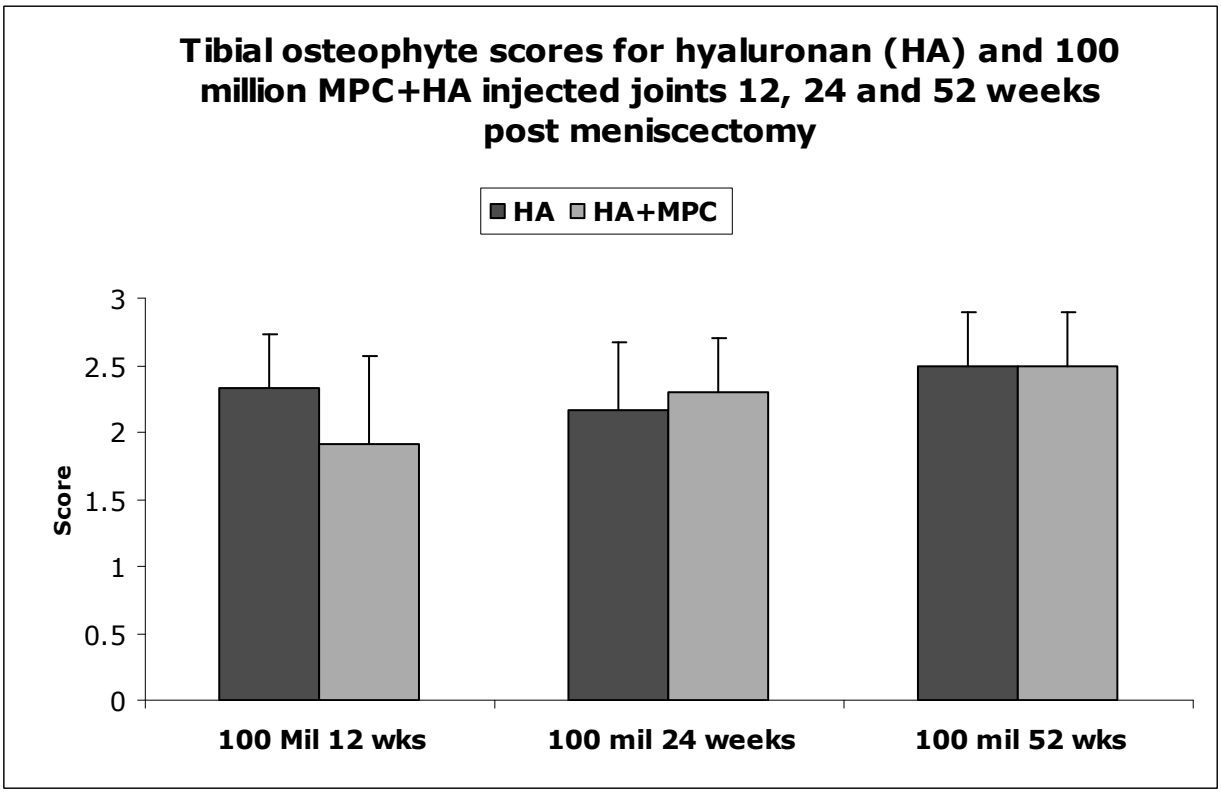

Tibial osteophyte scores for hyaluronan (HA) and 100 million MPC+HA injected joints 12, 24 and 52 weeks post meniscectomy
HA
HA+MPC
Score
3
2.5
2
1.5
1
0.5
0
100 Mil 12 wks
100 mil 24 weeks
100 mil 52 wks

Figure 8

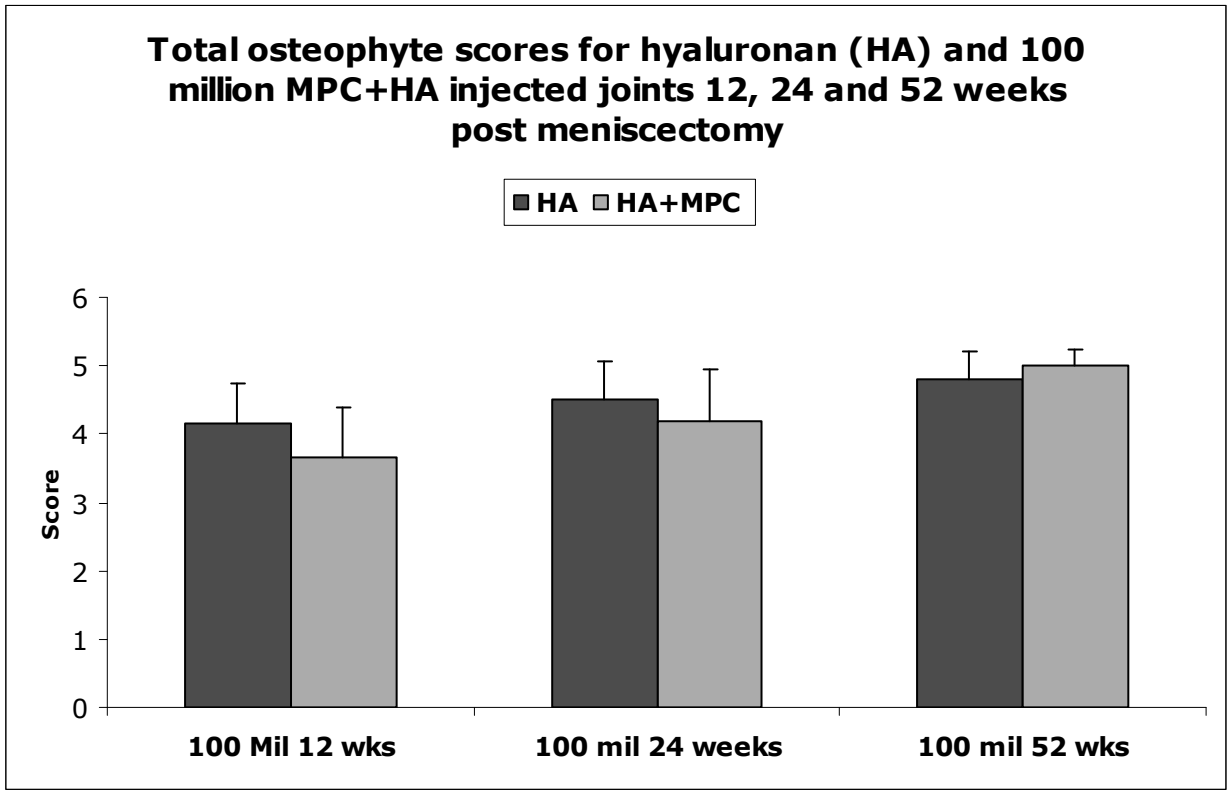


Figure 8 (continued)

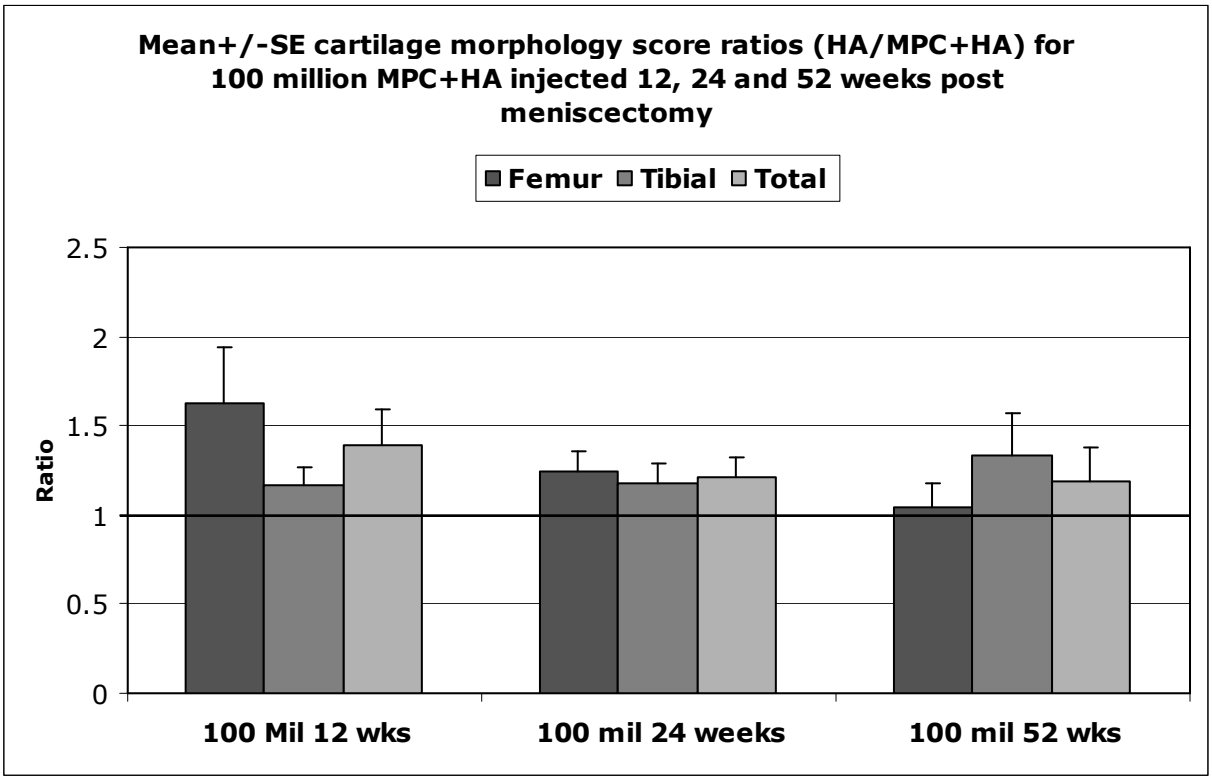

Mean+/-SE cartilage morphology score ratios (HA/MPC+HA) for 100 million MPC+HA injected 12, 24 and 52 weeks post meniscectomy
Femur
Tibial
Total
Ratio
2.5
2
1.5
1
0.5
0
100 Mil 12 wks
100 mil 24 weeks
100 mil 52 wks

Figure 9

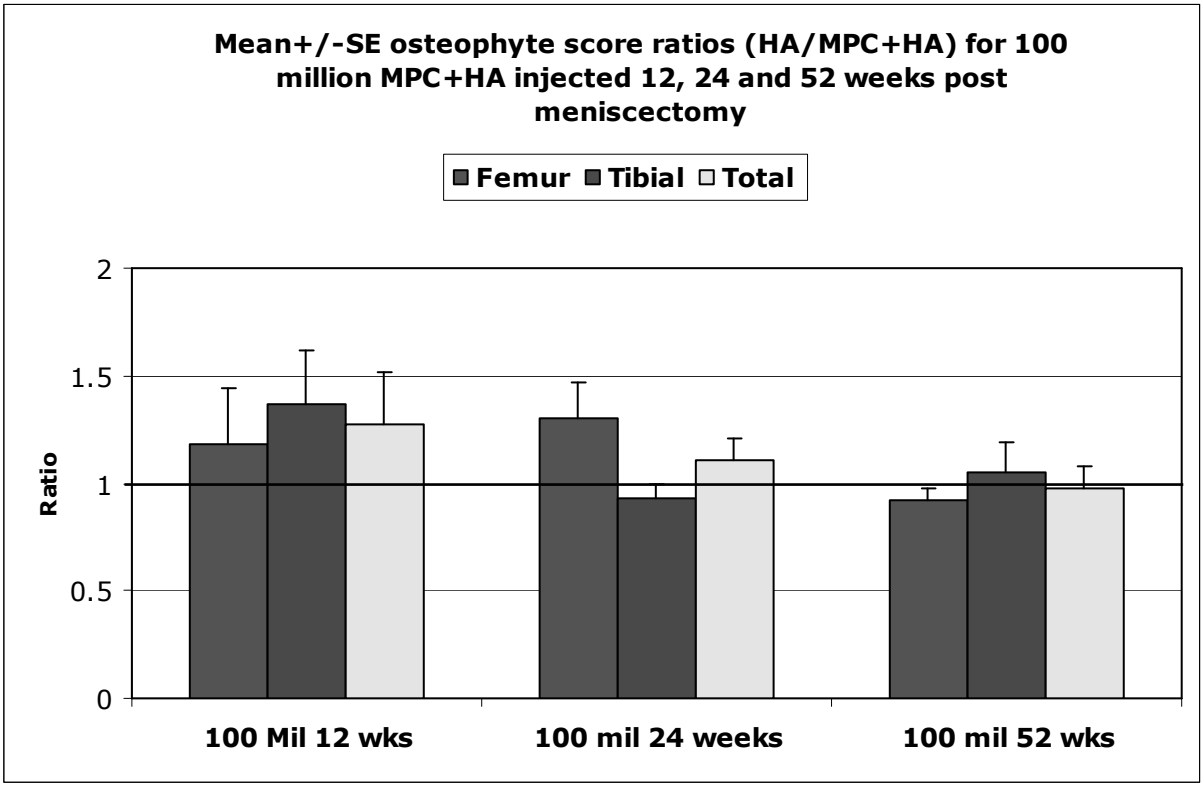

Mean+/-SE osteophyte score ratios (HA/MPC+HA) for 100 million MPC+HA injected 12, 24 and 52 weeks post meniscectomy
Femur
Tibial
Total
Ratio
2
1.5
1
0.5
0
100 Mil 12 wks
100 mil 24 weeks
100 mil 52 wks

Figure 10

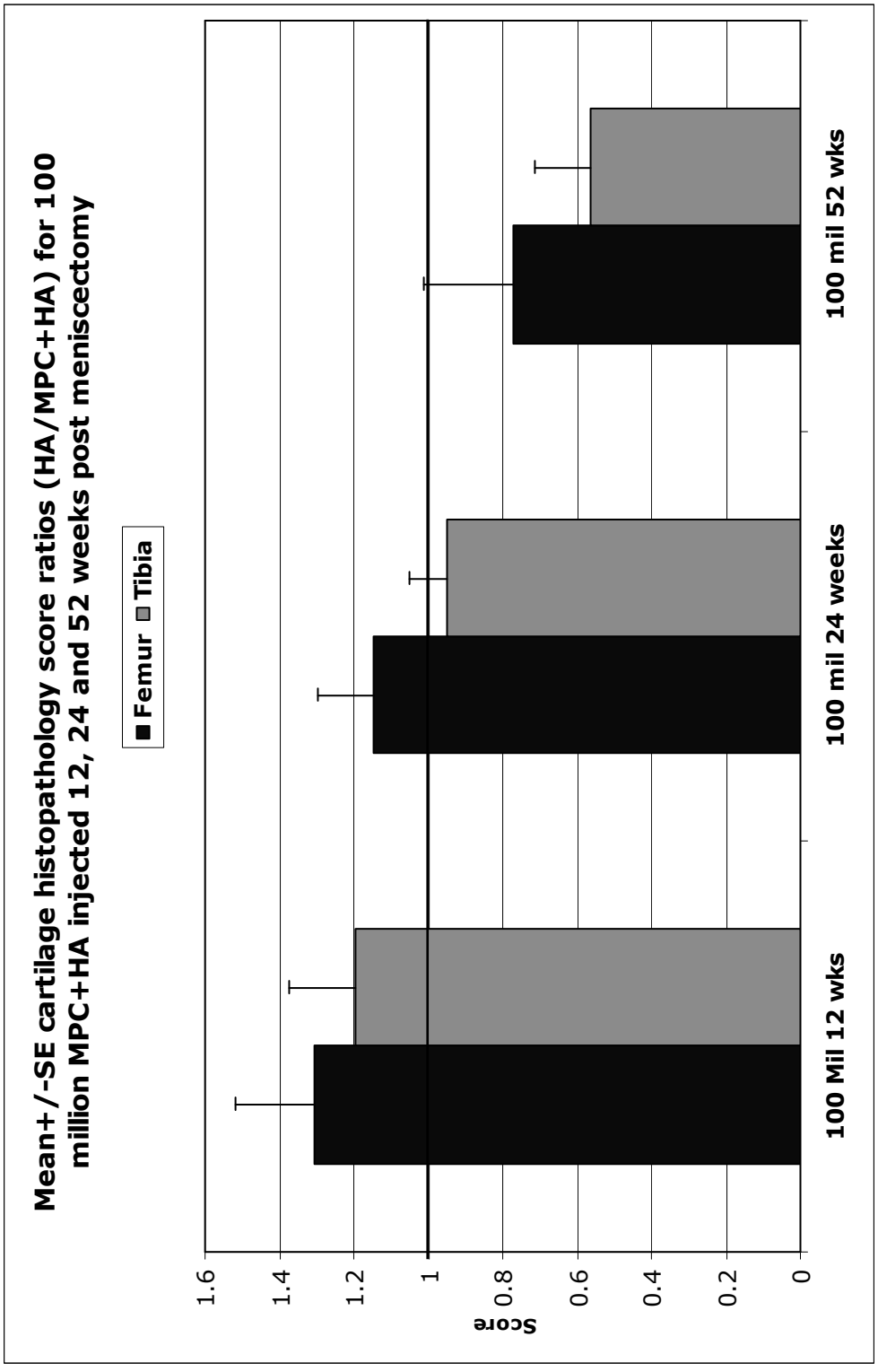

Mean+/-SE cartilage histopathology score ratios (HA/MPC+HA) for 100 million MPC+HA injected 12, 24 and 52 weeks post meniscectomy
Femur
Tibia
Score
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
100 Mil 12 wks
100 mil 24 weeks
100 mil 52 wks

Figure 11

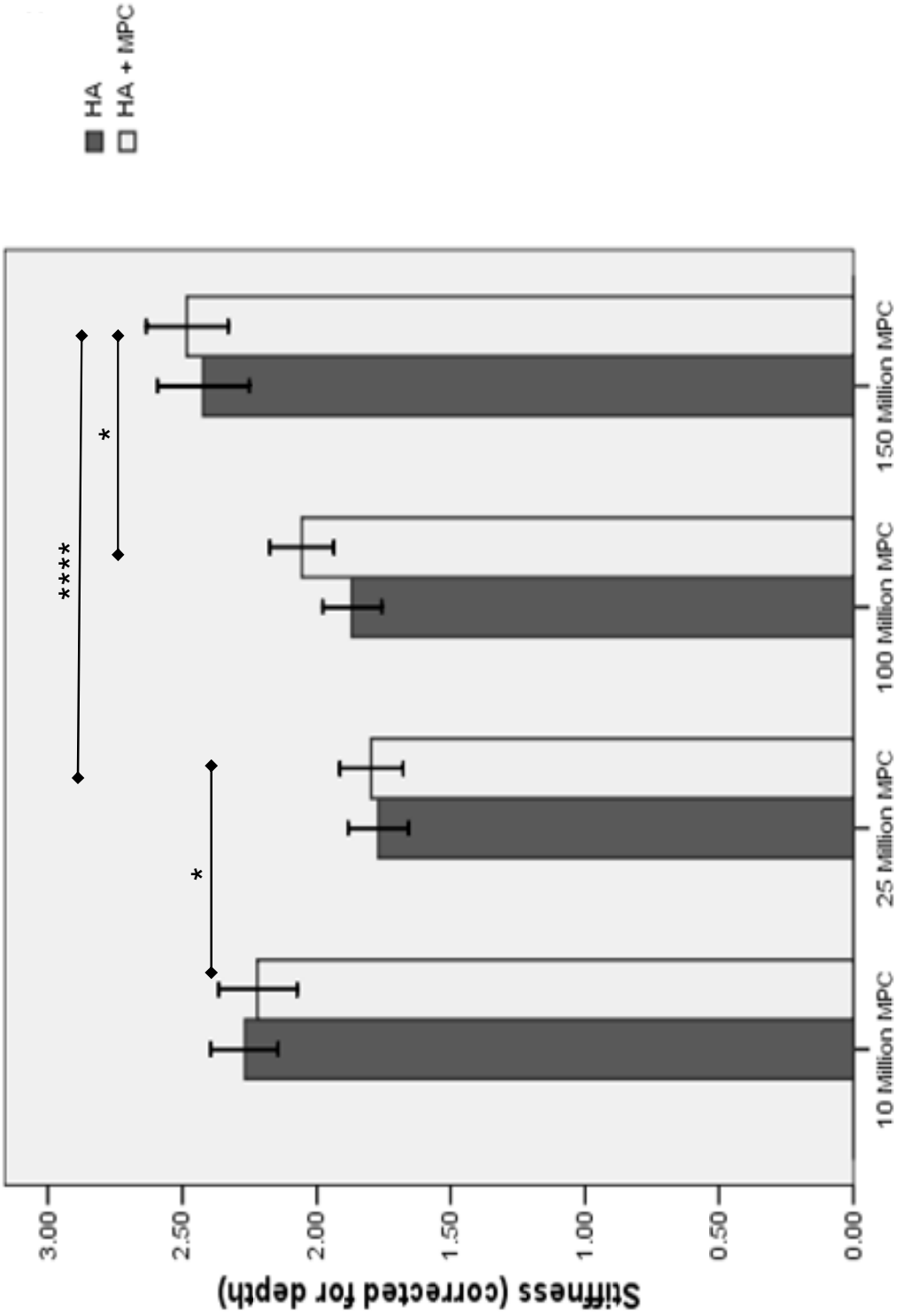

HA
HA + MPC
Stiffness (corrected for depth)
0.00
0.50
1.00
1.50
2.00
2.50
3.00
10 Million MPC
25 Million MPC
100 Million MPC
150 Million MPC
*
*
****

Figure 12

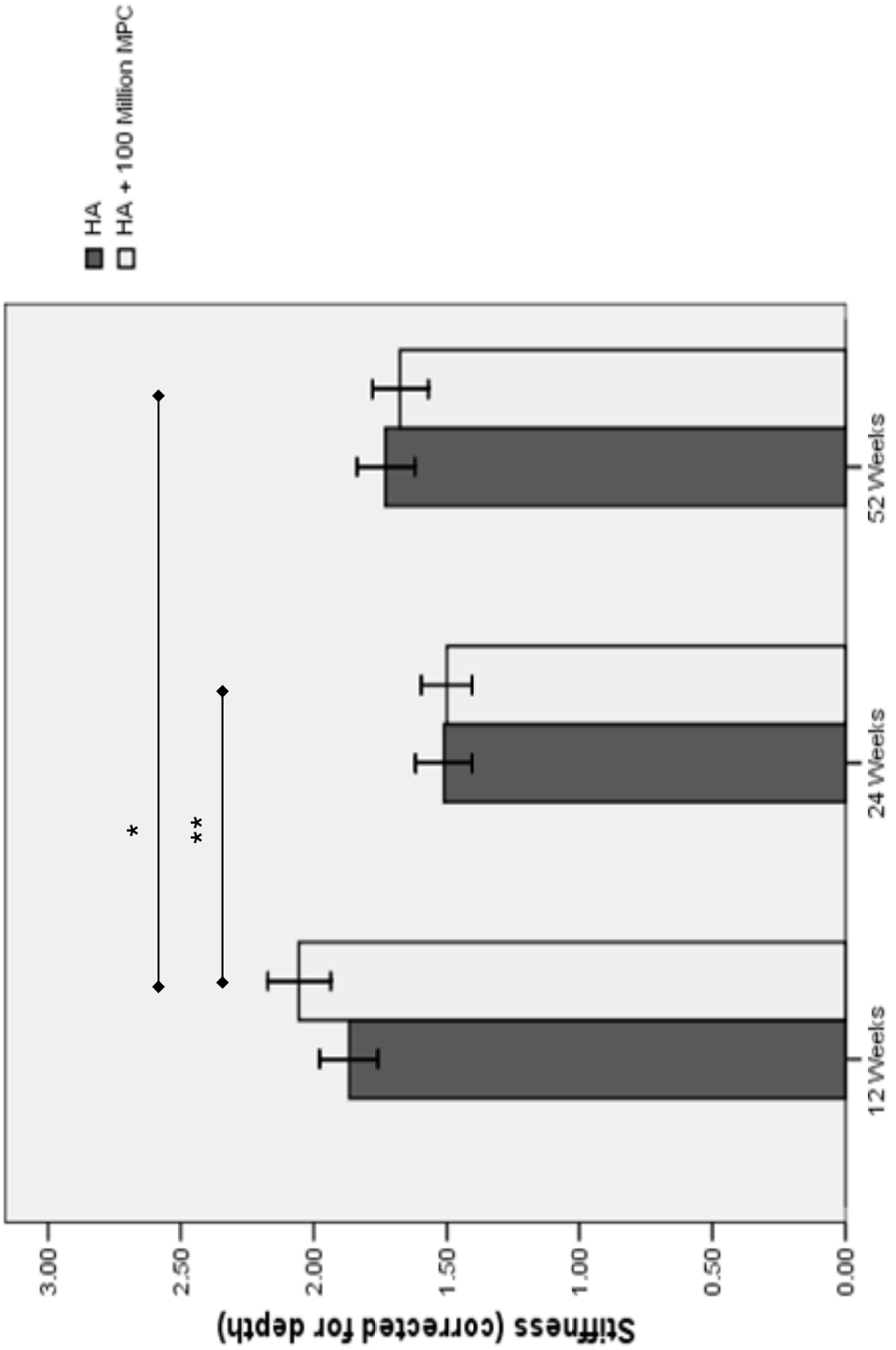

HA
HA + 100 Million MPC
Stiffness (corrected for depth)
3.00
2.50
2.00
1.50
1.00
0.50
0.00
12 Weeks
24 Weeks
52 Weeks
*
**

Figure 13

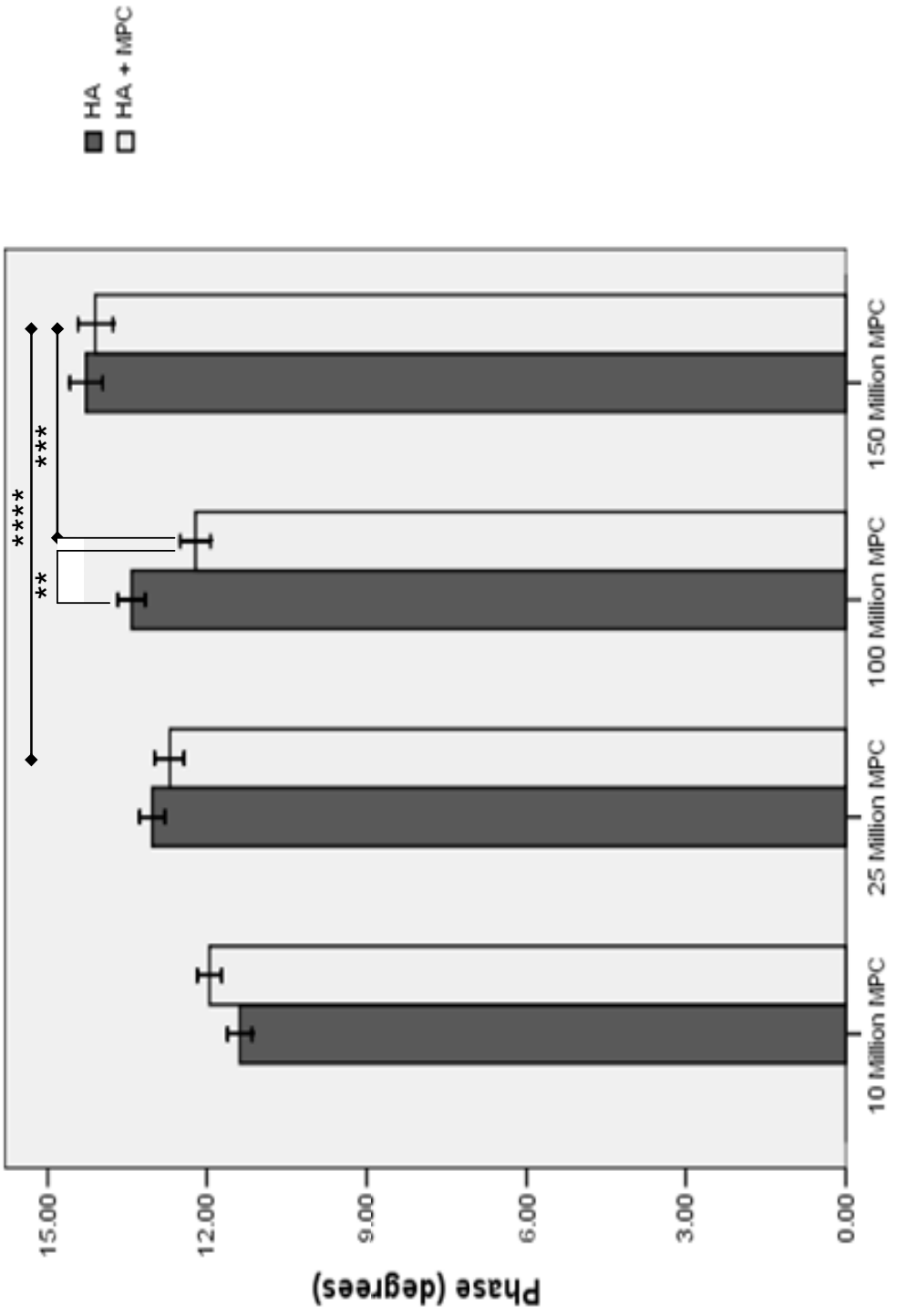

HA
HA + MPC
****
***
**
Phase (degrees)
15.00
12.00
9.00
6.00
3.00
0.00
10 Million MPC
25 Million MPC
100 Million MPC
150 Million MPC

Figure 14

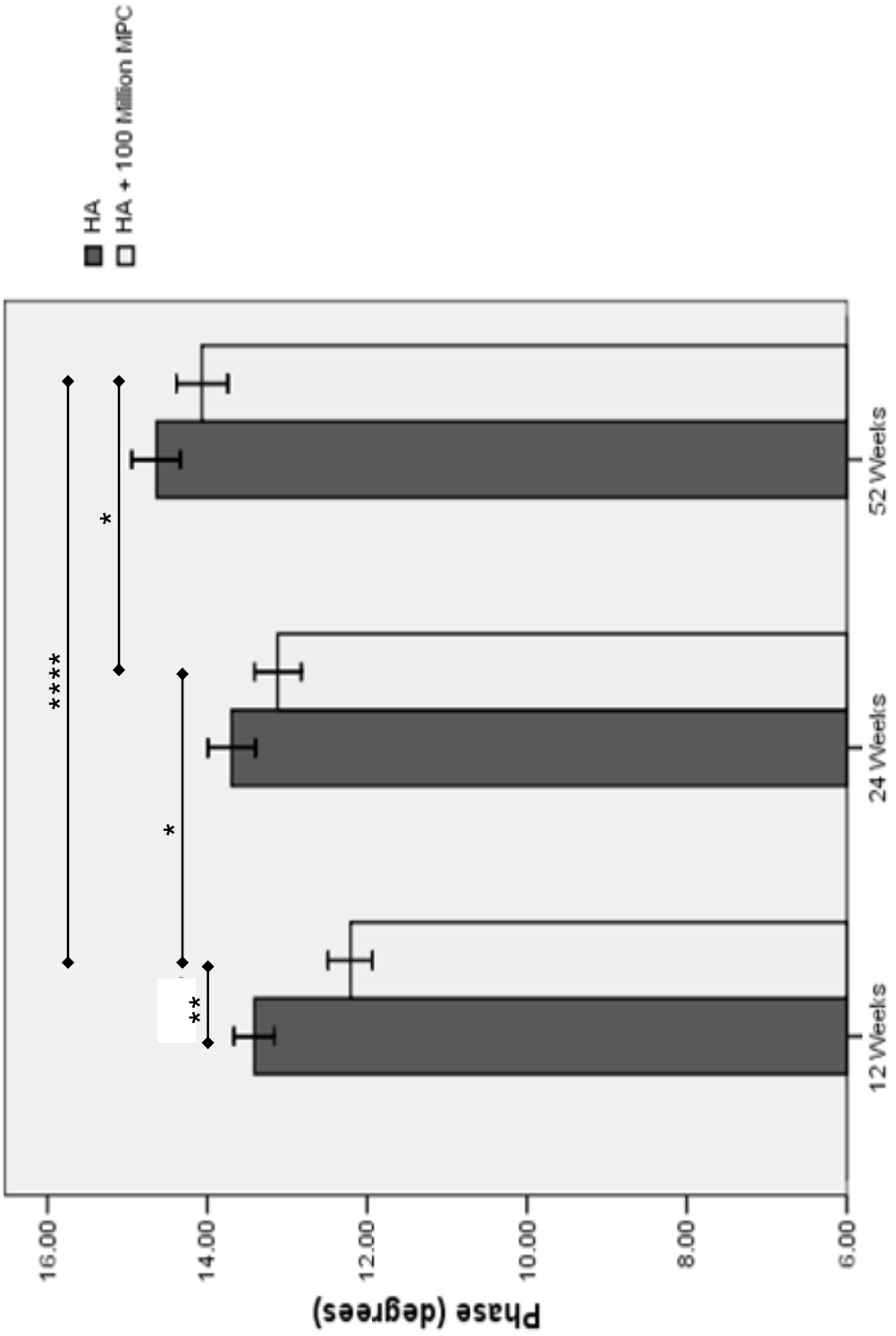

HA
HA + 100 Million MPC
Phase (degrees)
16.00
14.00
12.00
10.00
8.00
6.00
12 Weeks
24 Weeks
52 Weeks
**
*
*
****

Figure 15

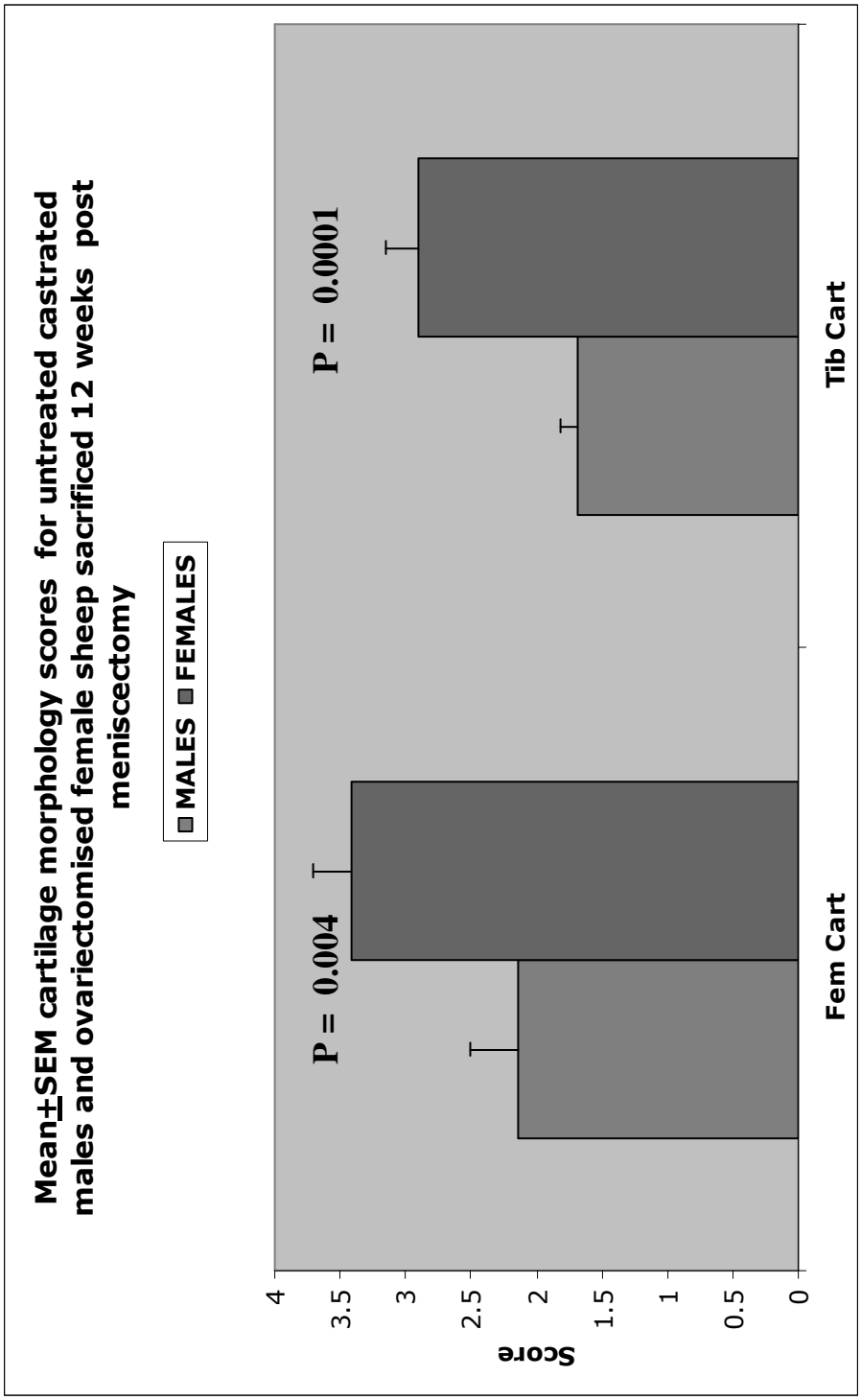

Mean±SEM cartilage morphology scores for untreated castrated males and ovariectomised female sheep sacrificed 12 weeks post meniscectomy
MALES
FEMALES
P = 0.004
P = 0.0001
Score
4
3.5
3
2.5
2
1.5
1
0.5
0
Fem Cart
Tib Cart

Figure 16

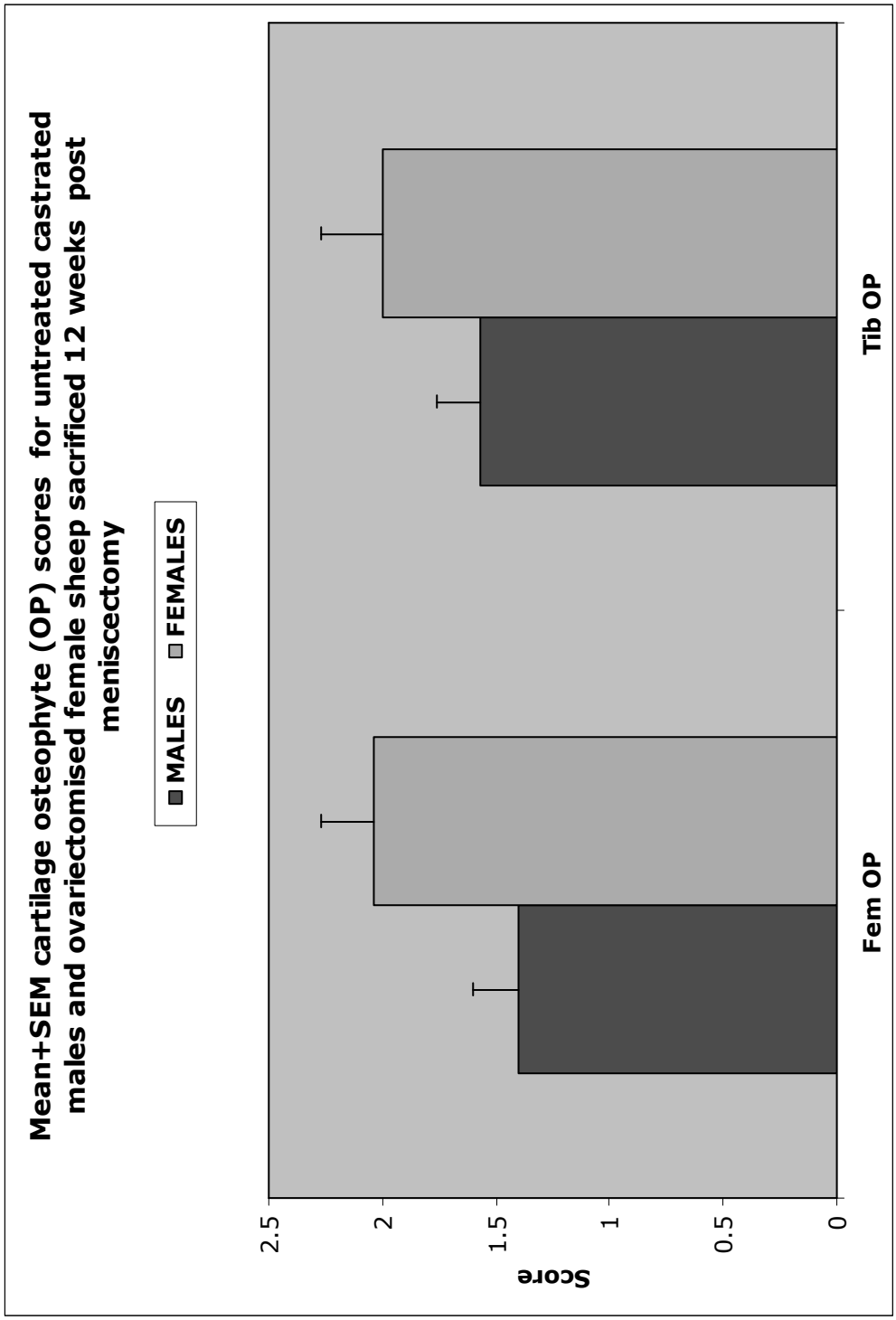

Mean+SEM cartilage osteophyte (OP) scores for untreated castrated males and ovariectomised female sheep sacrificed 12 weeks post meniscectomy
MALES
FEMALES
Score
2.5
2
1.5
1
0.5
0
Fem OP
Tib OP

Figure 17

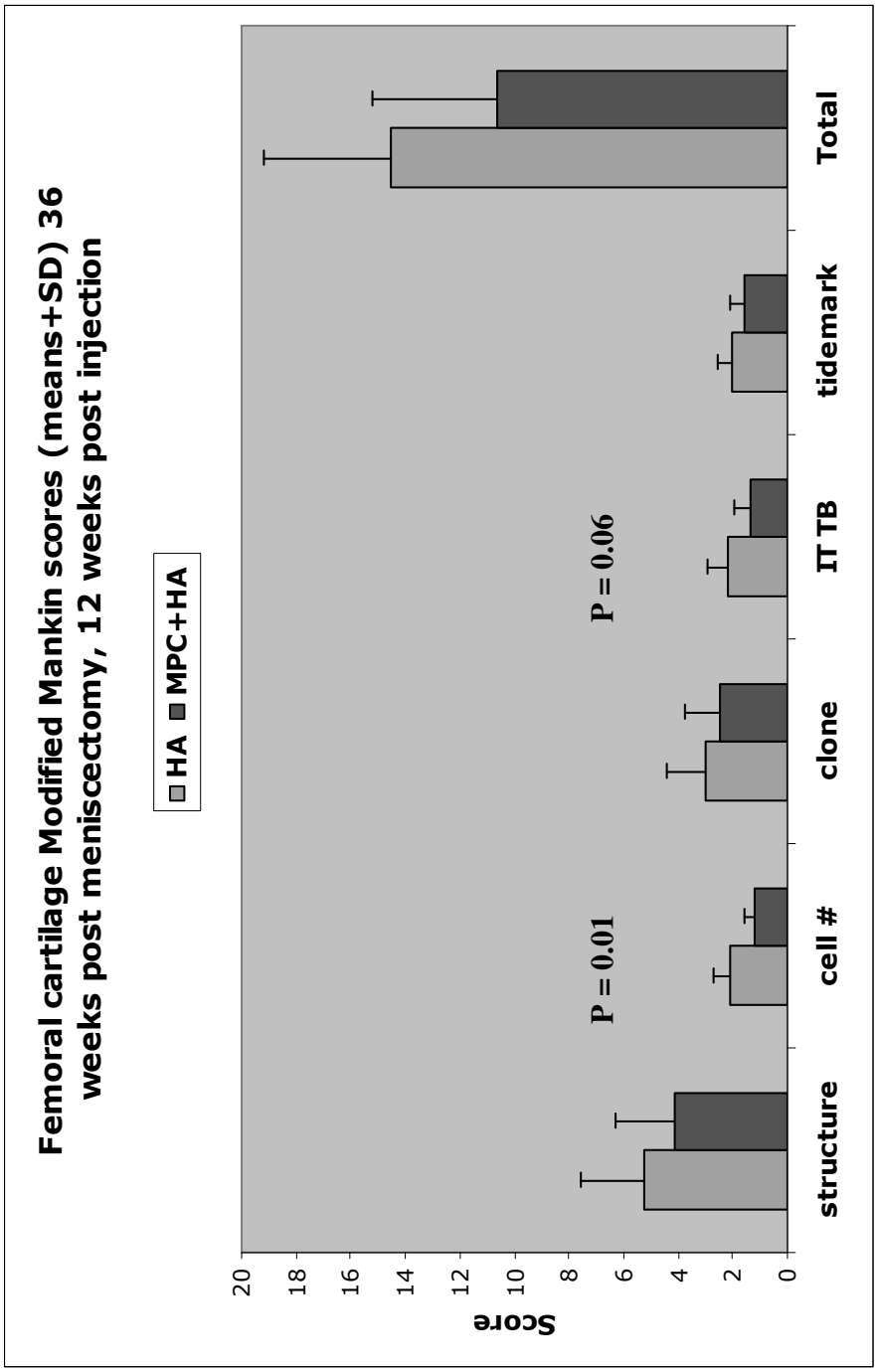

Femur
Femoral cartilage Modified Mankin scores (means+SD) 36 weeks post meniscectomy, 12 weeks post injection
HA
MPC+HA
Score
20
18
16
14
12
10
8
6
4
2
0
P = 0.01
P = 0.06
structure
cell #
clone
IT TB
tidemark
Total
HA Score > MPC Score

Figure 18

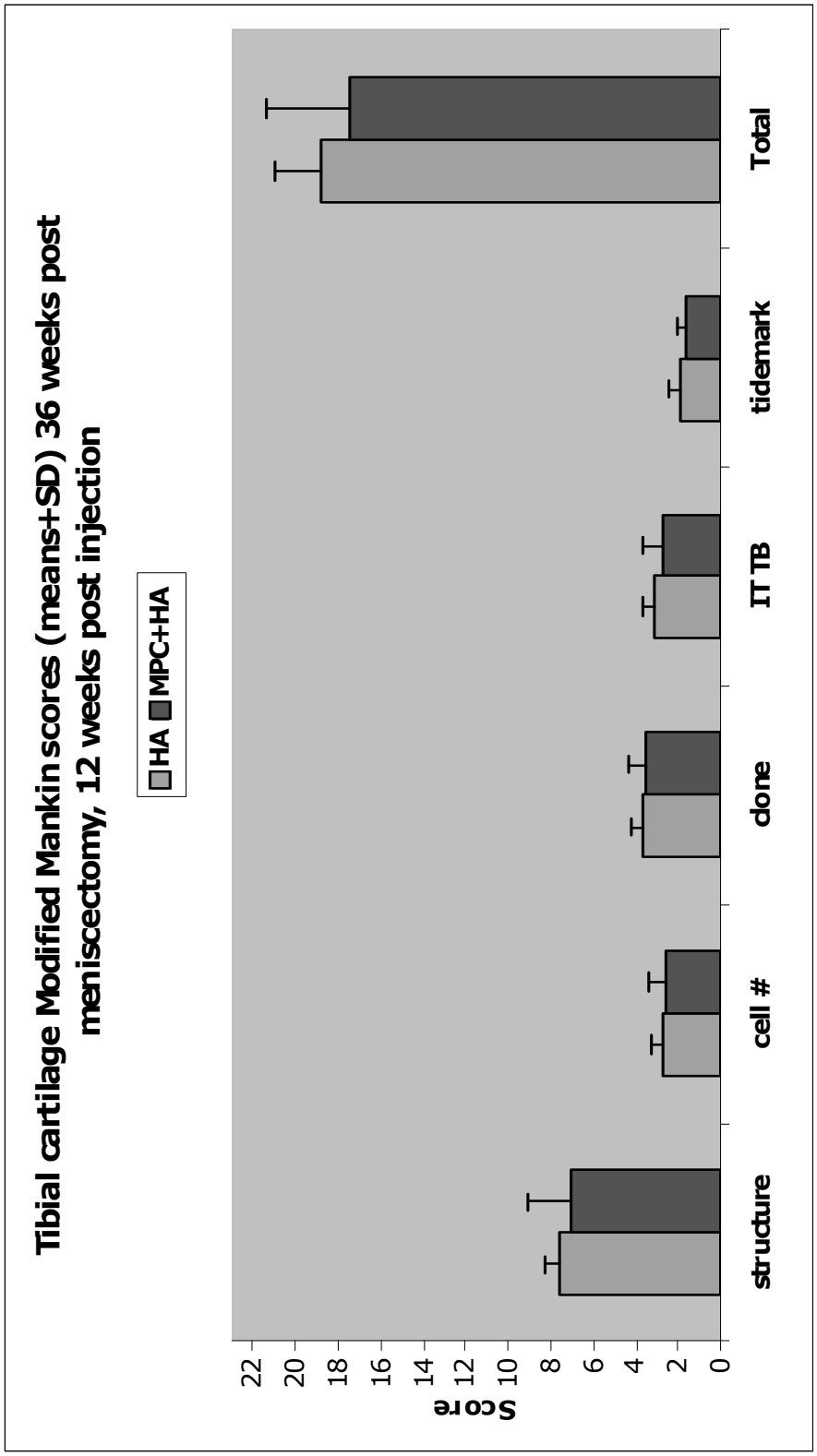


Figure 18 (continued)

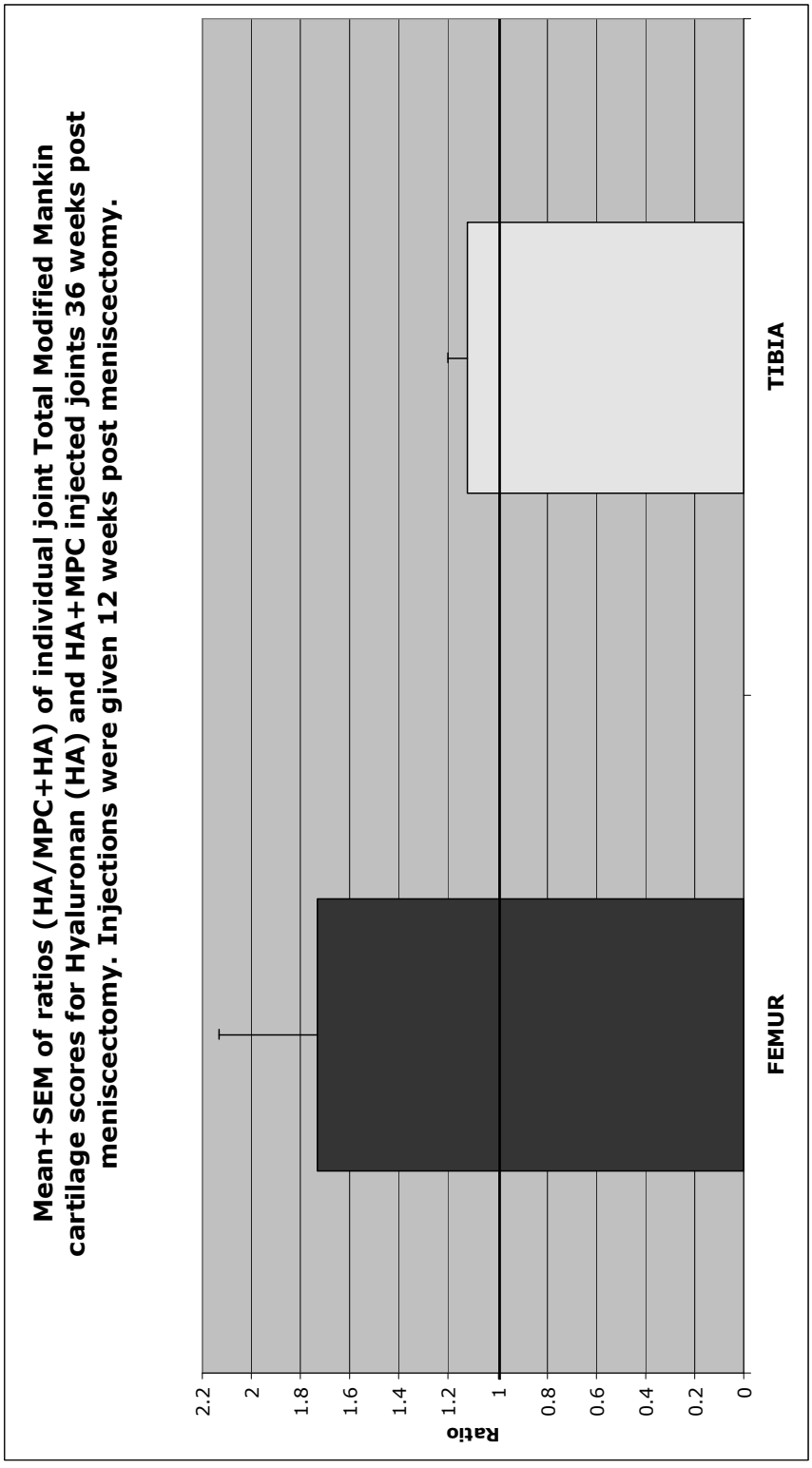
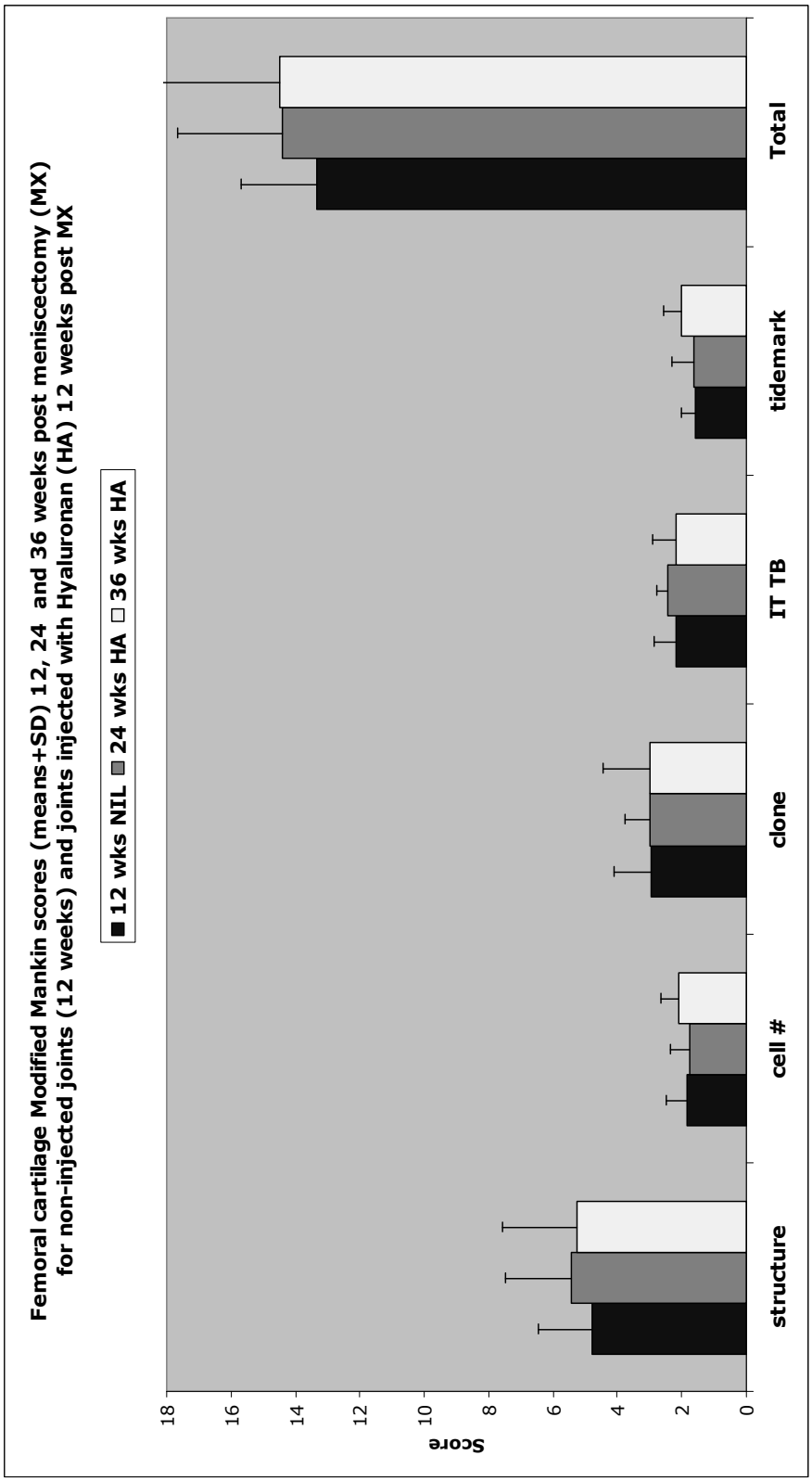

Mean+SEM of ratios (HA/MPC+HA) of individual joint Total Modified Mankin cartilage scores for Hyaluronan (HA) and HA+MPC injected joints 36 weeks post meniscectomy. Injections were given 12 weeks post meniscectomy.
Ratio
2.2
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
FEMUR
TIBIA

Figure 19


Femoral cartilage Modified Mankin scores (means+SD) 12, 24 and 36 weeks post meniscectomy (MX)
for non-injected joints (12 weeks) and joints injected with Hyaluronan (HA) 12 weeks post MX
12 wks NIL
24 wks HA
36 wks HA
Score
0
2
4
6
8
10
12
14
16
18
structure
cell #
clone
IT TB
tidemark
Total

HA

Figure 20

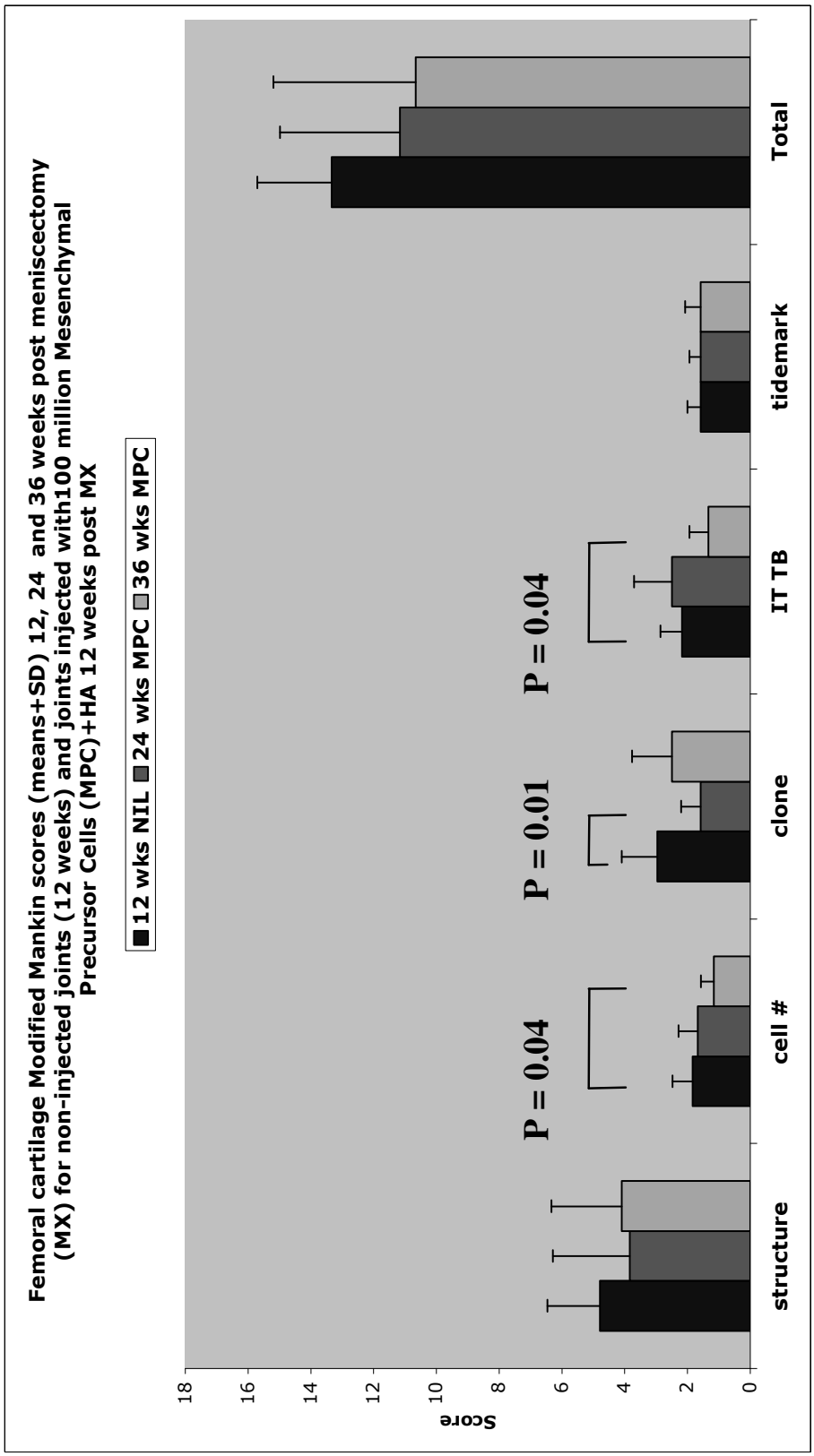


Figure 20 (continued)

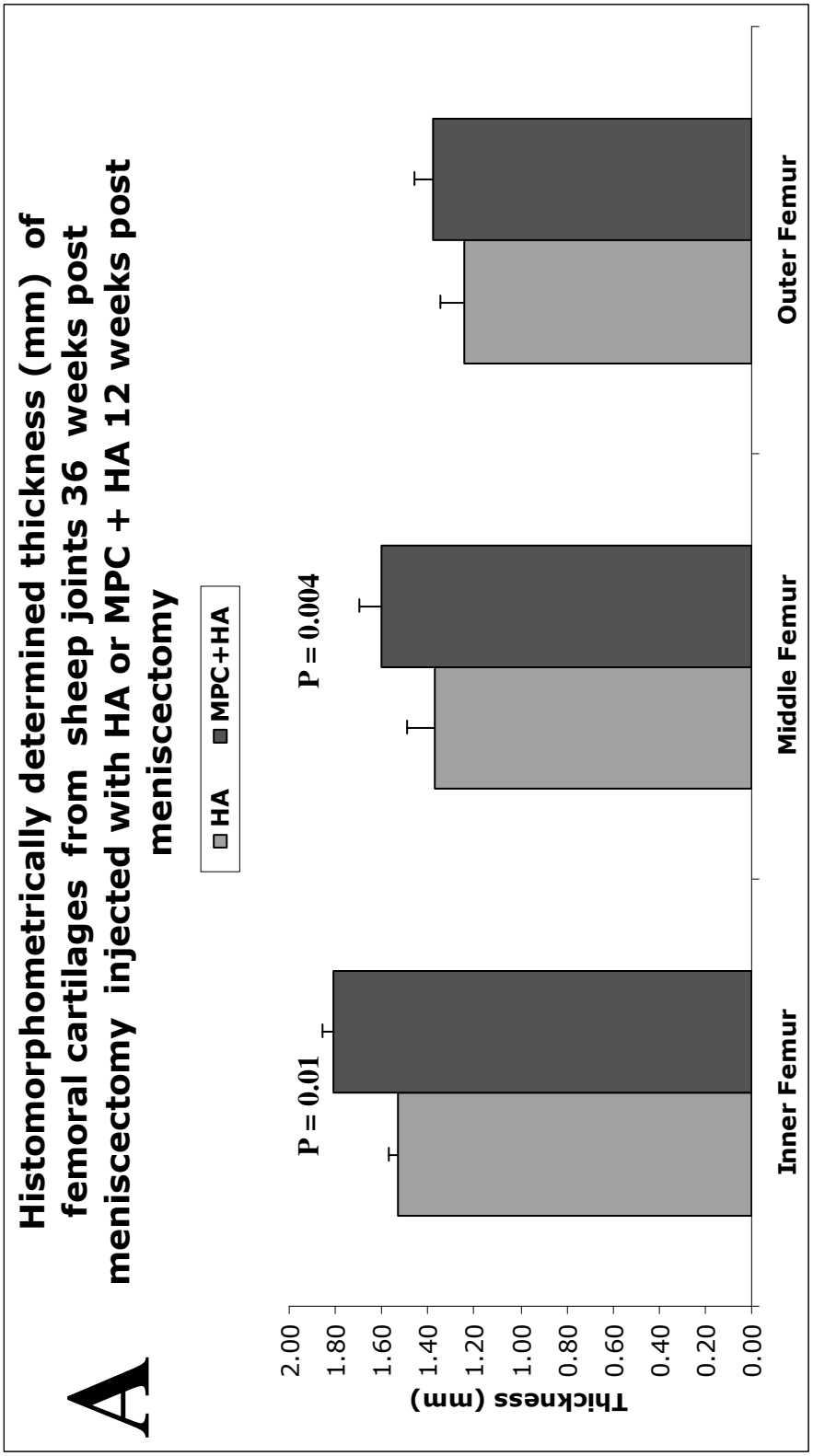

A
Histomorphometrically determined thickness (mm) of femoral cartilages from sheep joints 36 weeks post meniscectomy injected with HA or MPC + HA 12 weeks post meniscectomy
HA
MPC+HA
P = 0.01
P = 0.004
Thickness (mm)
2.00
1.80
1.60
1.40
1.20
1.00
0.80
0.60
0.40
0.20
0.00
Inner Femur
Middle Femur
Outer Femur

Figure 21

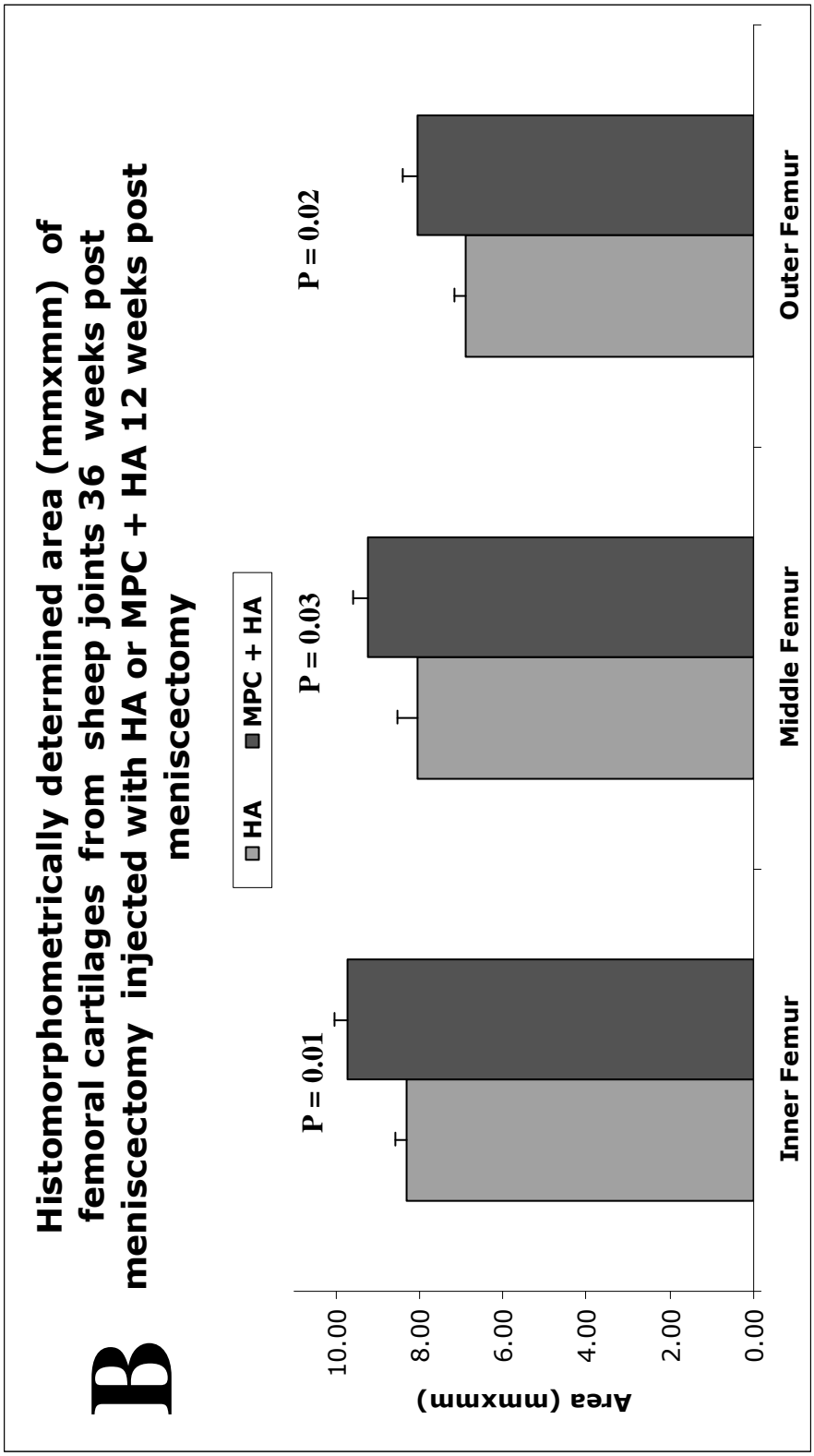


Figure 21 (continued)

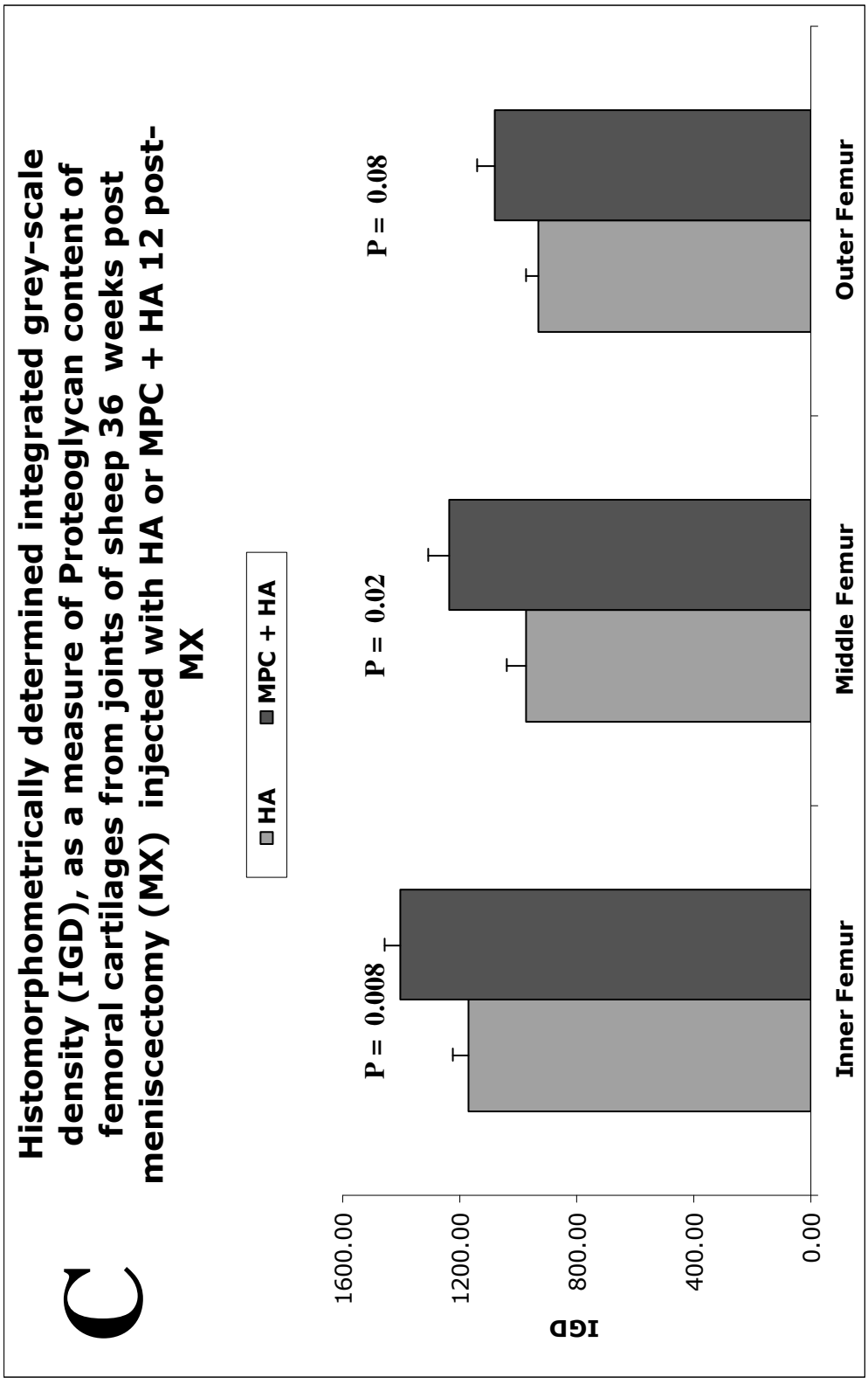


Figure 21 (continued)

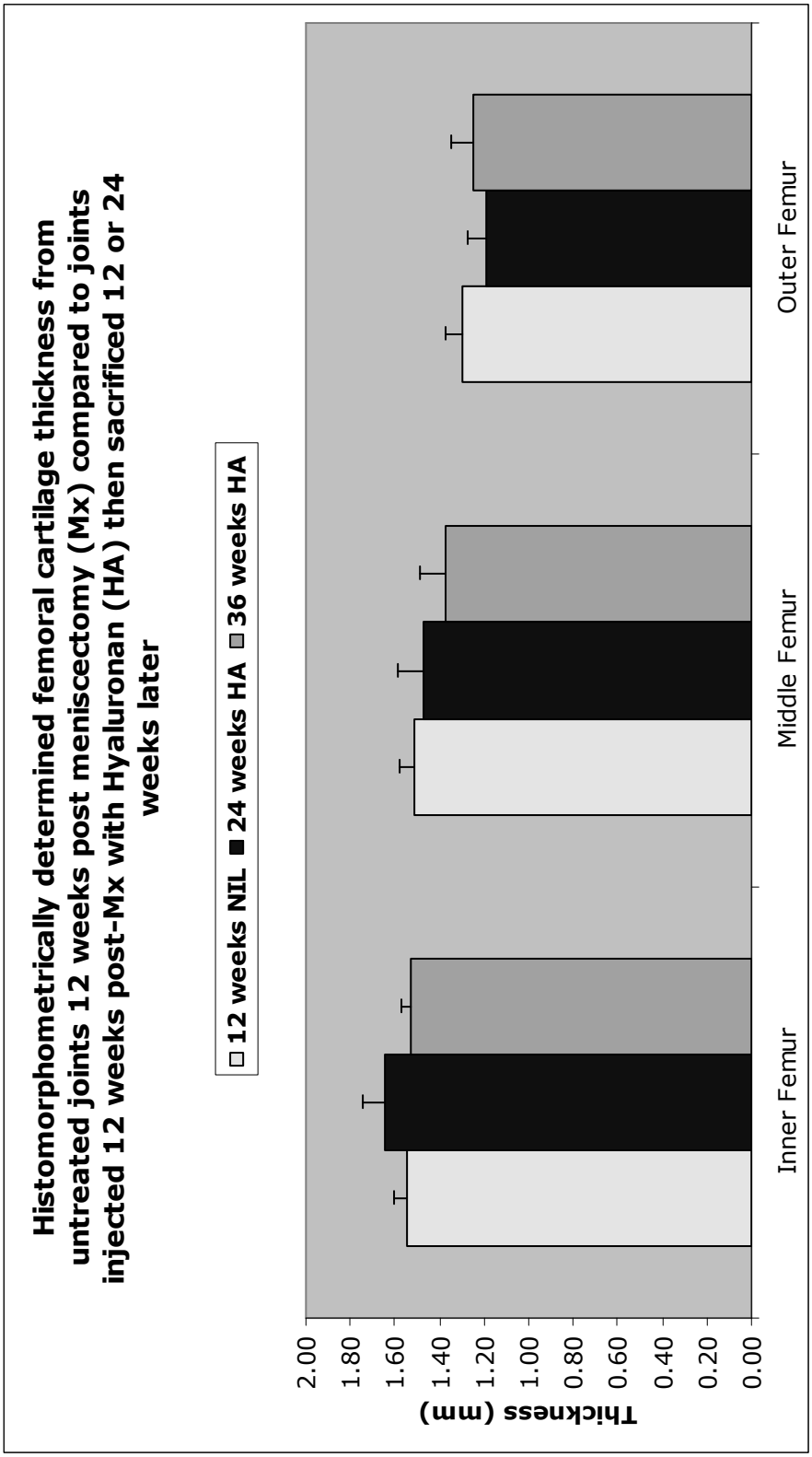

Histomorphometrically determined femoral cartilage thickness from untreated joints 12 weeks post meniscectomy (Mx) compared to joints injected 12 weeks post-Mx with Hyaluronan (HA) then sacrificed 12 or 24 weeks later
12 weeks NIL
24 weeks HA
36 weeks HA
Thickness (mm)
2.00
1.80
1.60
1.40
1.20
1.00
0.80
0.60
0.40
0.20
0.00
Inner Femur
Middle Femur
Outer Femur
HA

Figure 22

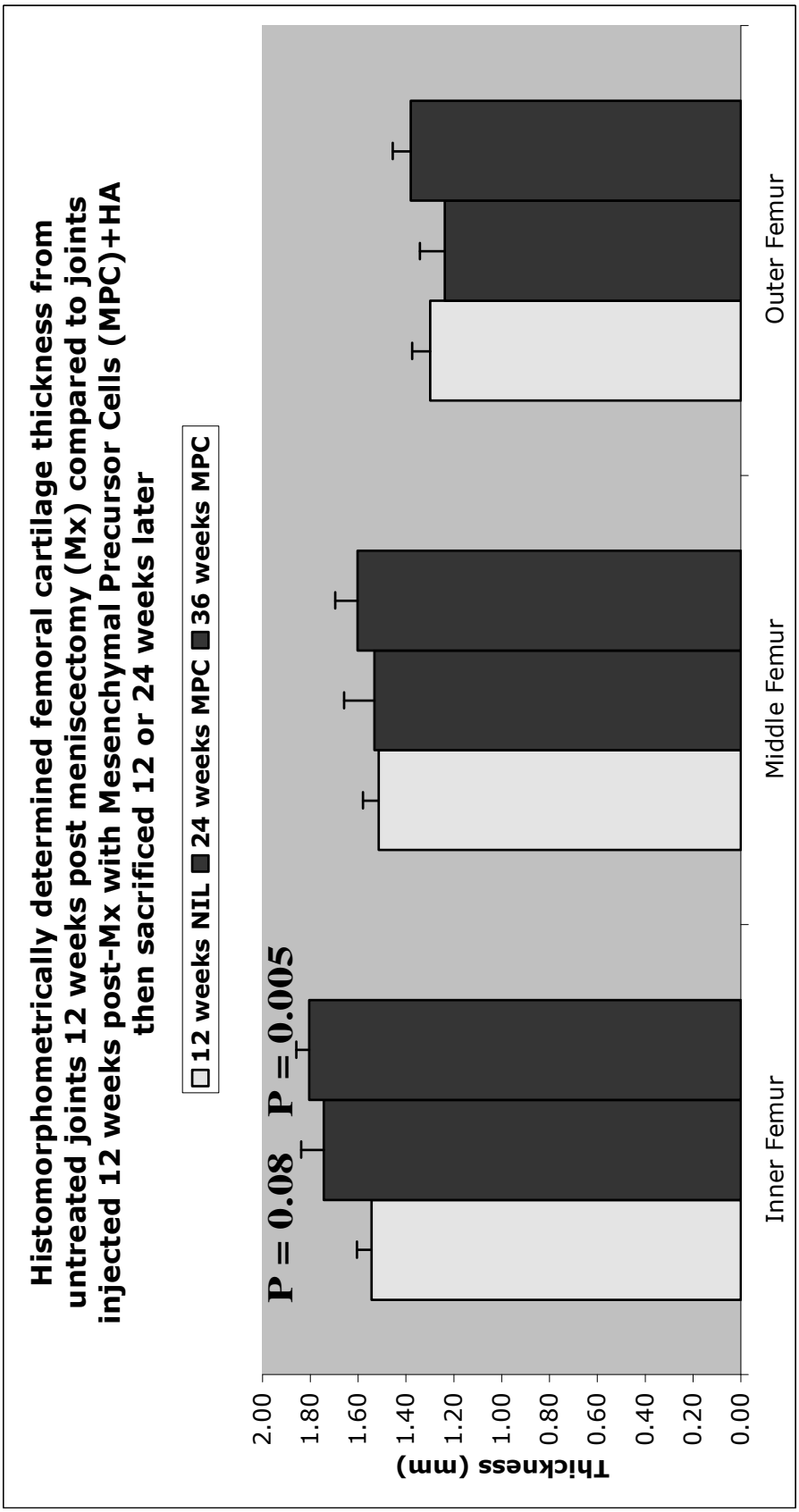


Figure 22 (continued)

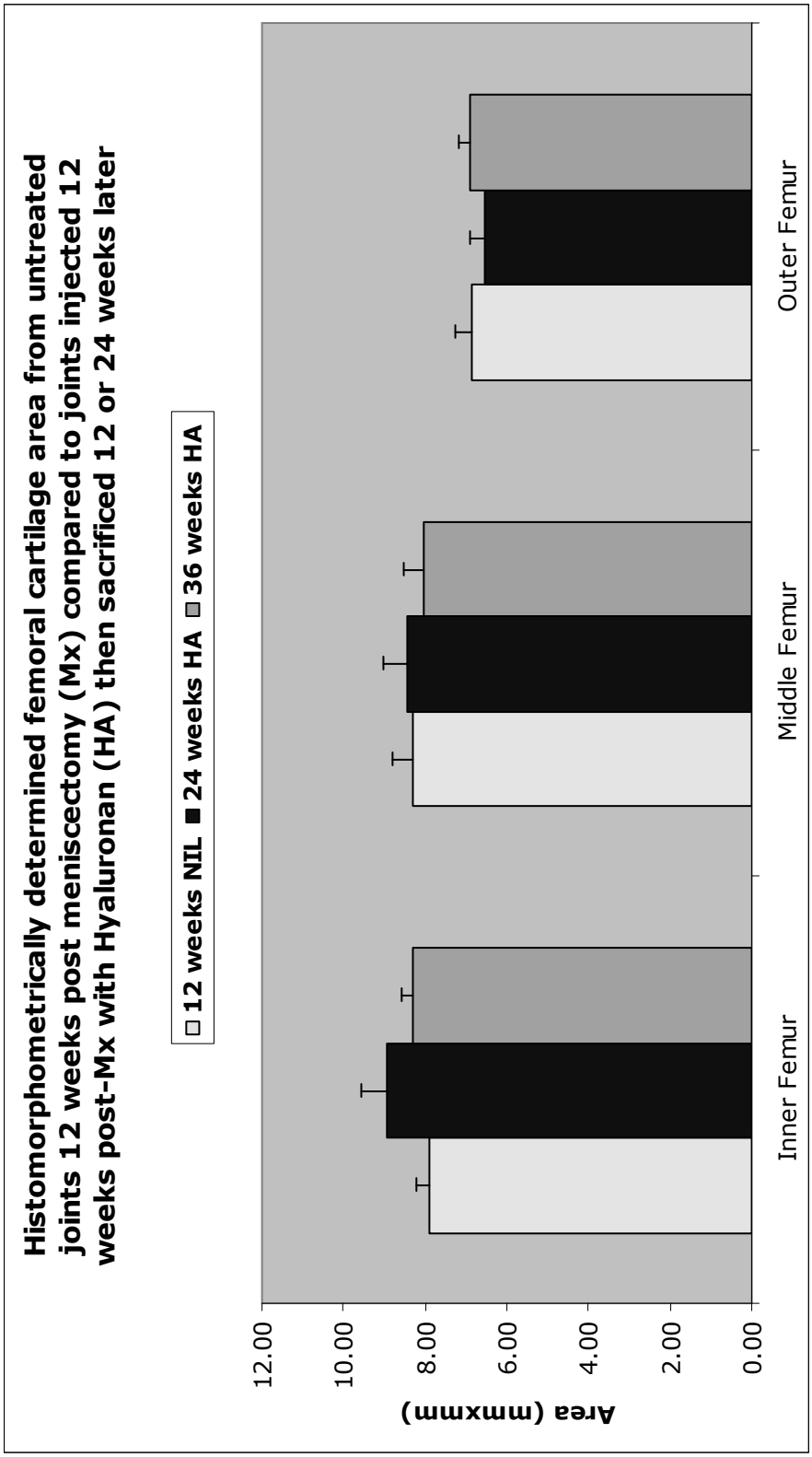

Histomorphometrically determined femoral cartilage area from untreated joints 12 weeks post meniscectomy (Mx) compared to joints injected 12 weeks post-Mx with Hyaluronan (HA) then sacrificed 12 or 24 weeks later
12 weeks NIL
24 weeks HA
36 weeks HA
Area (mmxmm)
12.00
10.00
8.00
6.00
4.00
2.00
0.00
Inner Femur
Middle Femur
Outer Femur
HA

Figure 23

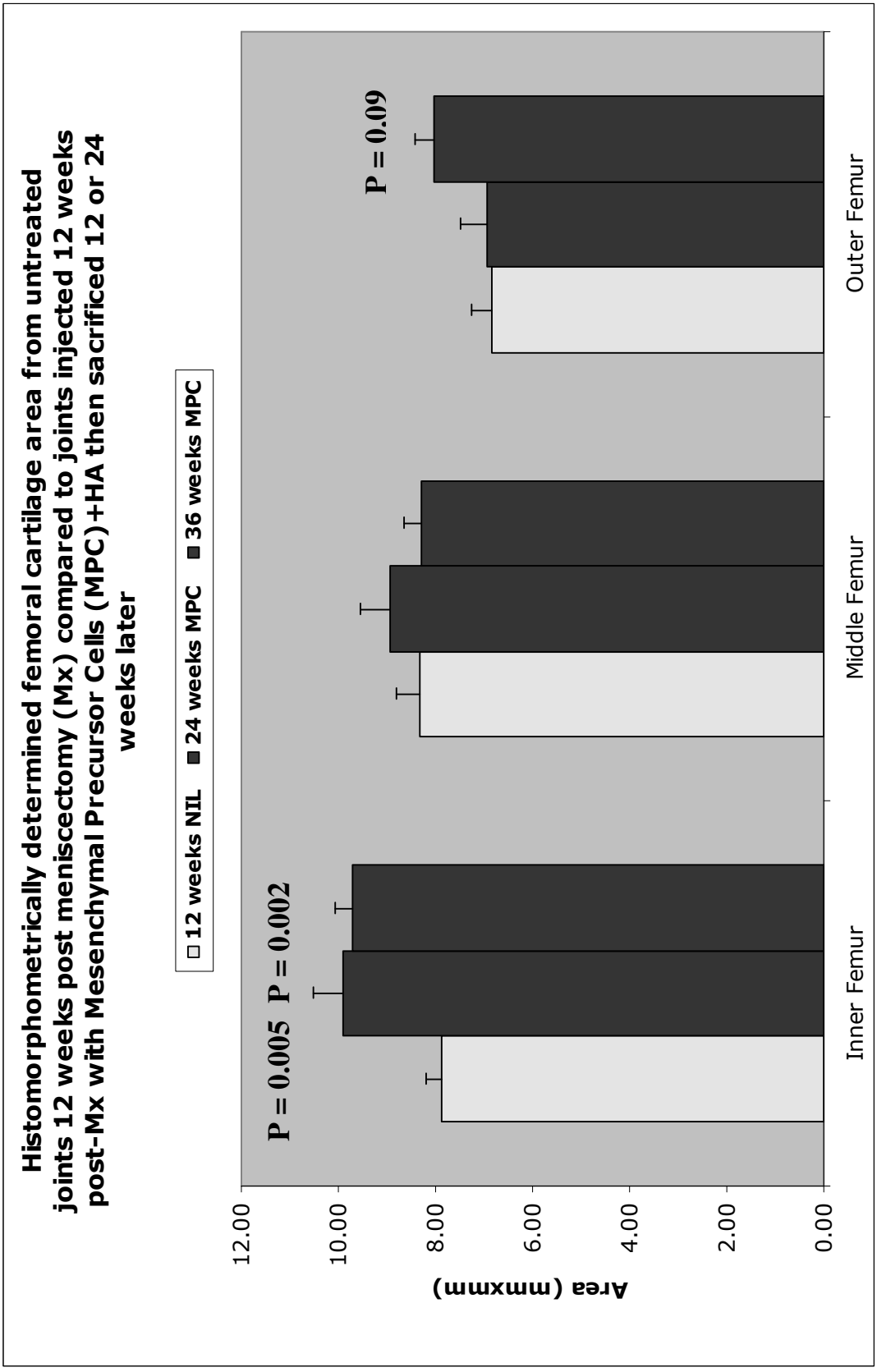


Figure 23 (continued)

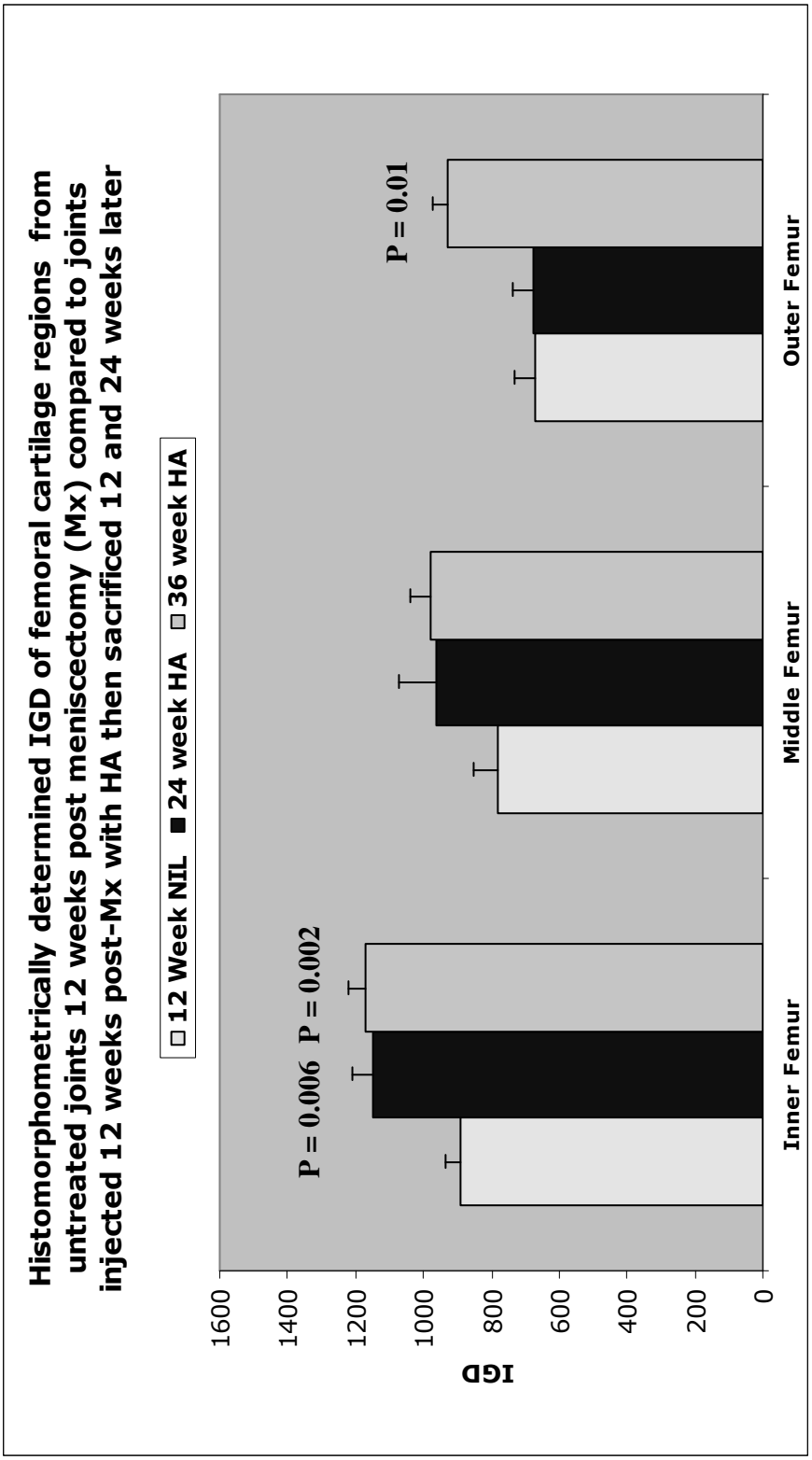

Histomorphometrically determined IGD of femoral cartilage regions from untreated joints 12 weeks post meniscectomy (Mx) compared to joints injected 12 weeks post-Mx with HA then sacrificed 12 and 24 weeks later
12 Week NIL
24 week HA
36 week HA
IGD
1600
1400
1200
1000
800
600
400
200
0
P = 0.006
P = 0.002
P = 0.01
Inner Femur
Middle Femur
Outer Femur
HA

Figure 24

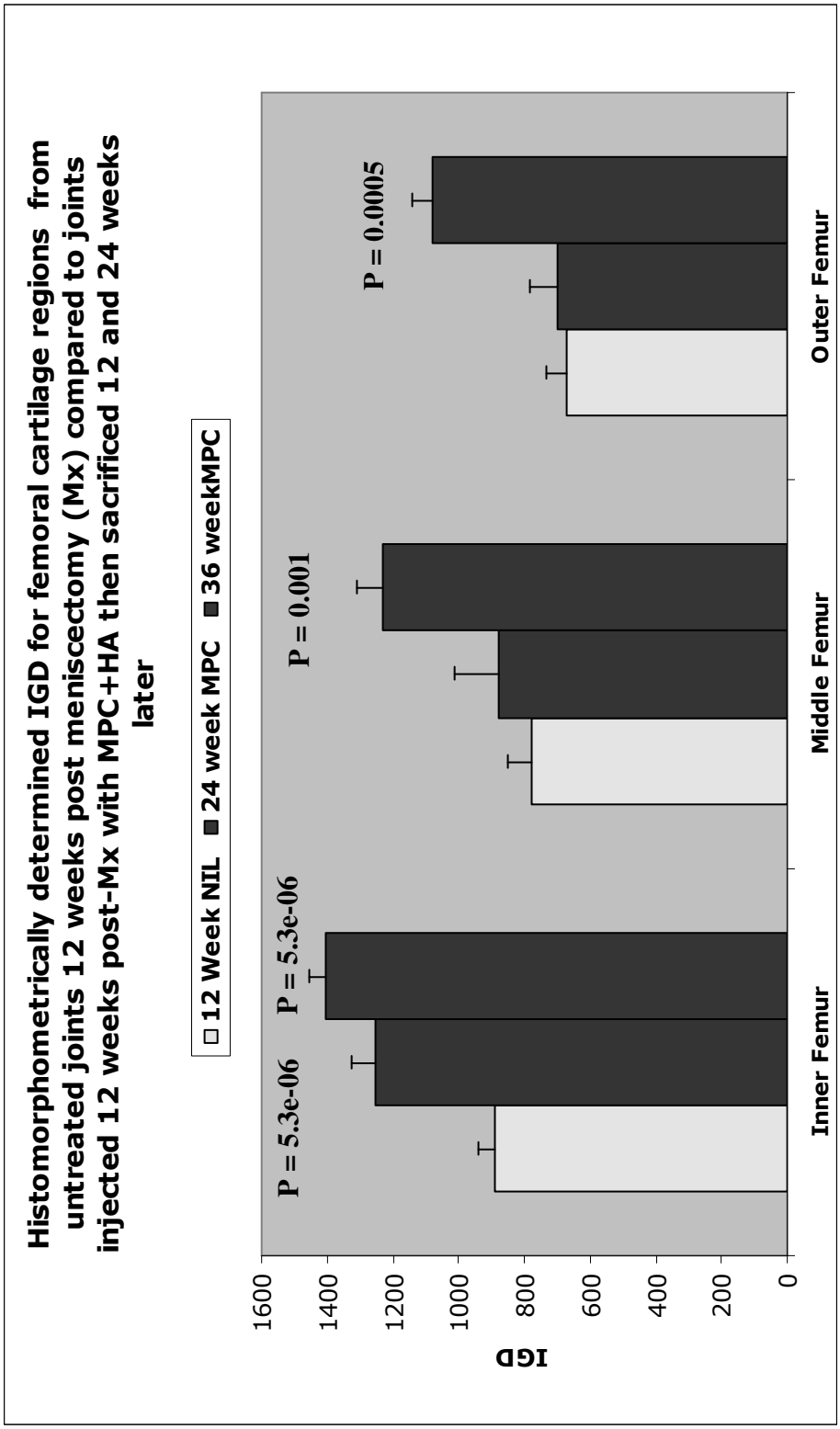


Figure 24 (continued)

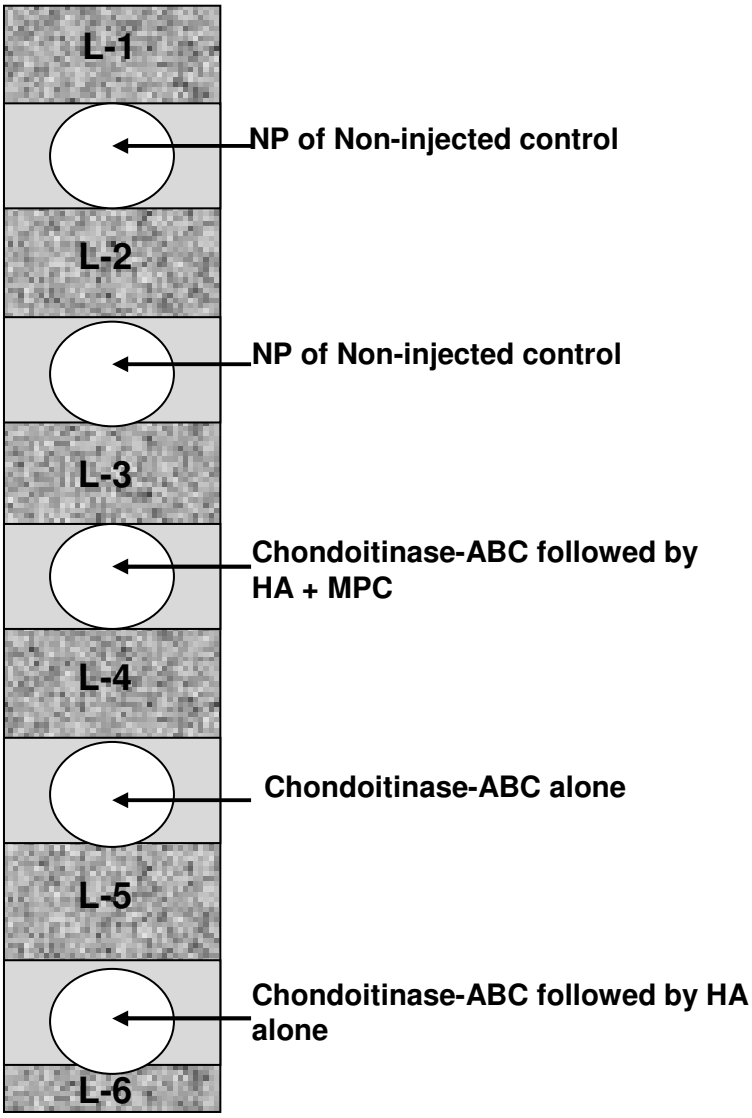

L-1
NP of Non-injected control
L-2
NP of Non-injected control
L-3
Chondoitinase-ABC followed by HA + MPC
L-4
Chondoitinase-ABC alone
L-5
Chondoitinase-ABC followed by HA alone
L-6

Figure 25

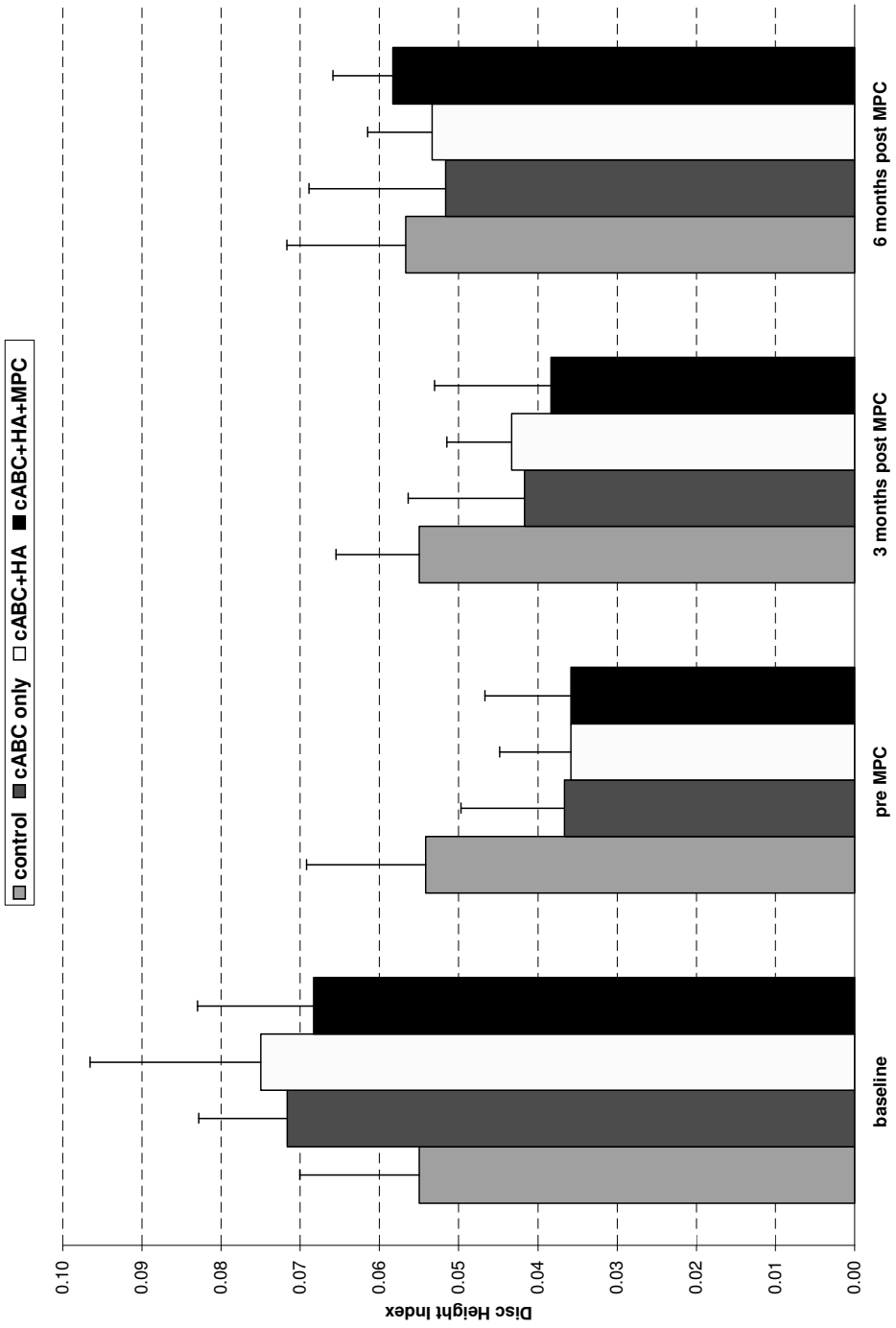

control
cABC only
cABC+HA
cABC+HA+MPC
Disc Height Index
0.10
0.09
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0.00
baseline
pre MPC
3 months post MPC
6 months post MPC

Figure 26