Author, Year Country Study Design Sample Size	Population Intervention Outcome Measure	Results
	Bone Composition and Osteoporosis	
(Zebracki et al., 2013b) USA Observational N=279	**Population:** Age: 14.9±4.9 yr; Gender: males=46, females=36; Time since injury: 4.3±3.3 yr; Level of injury: paraplegia=50, tetraplegia=32; Severity of injury: AIS A=34. **Intervention:** None. Chart review. **Outcome Measures:** Serum 25(OH) D level.	1. Serum 25(OH) D levels ranged from 4.1 to 89.4 ng/ml with a mean of 24.7ng/ml (SD=13.1). 2. Most of the youth demonstrated vitamin D deficiency (39%) or insufficiency (40%), whereas only 21% had sufficient levels of vitamin D. 3. There was no difference in vitamin D status as a function of gender or injury level. 4. Vitamin D status differed by age groups ($p<0.05$); although the percent sufficient was similar for the two age groups, the percent deficient relative to the percent insufficient was greater in the '13-21 yr' age group.
(Biggin et al., 2013) Australia Observational N=19	**Population:** Age: 6.6±4.1 yr; Gender: males=10, females=9; Injury etiology: traumatic=10, non-traumatic=9; Time since injury: 5.6±3.6 yr; Level of injury: C3-4=5, C5-7=5, T1-6=6, T7-12=3; Severity of injury: complete tetraplegia=5, incomplete tetraplegia=5, complete paraplegia=6, incomplete paraplegia=3. **Intervention:** None. Chart review. **Outcome Measures:** Using Peripheral Quantitative Computer Tomography (pQCT) the following measurements were made: volumetric Bone Mineral Density (vBMD, mg/cm^3), total and Cortical Cross-sectional Area (CSA, mm^2), Muscle CSA (mm^2), total and cortical Bone Mineral Content (BMC, mg/mm) and polar SSI (pSSI, mm^3)	1. There was no statistical difference in the radial data from those with paraplegia compared to able-body control data. 2. In the radius of subjects with tetraplegia, there was a significant reduction in BMC at both the metaphysis and diaphysis ($p<0.05$ for both), trabecular vBMD was significantly reduced, and cortical vBMD was indistinguishable from able-bodied controls; total CSA at the radial metaphyseal site and diaphyseal sites was reduced ($p<0.05$ for both). 3. In the tibia, there was no statistical difference between those with paraplegia versus tetraplegia so data were pooled. 4. vBMD of the metaphysis showed significant reduction ($p<0.05$). 5. In the tibial diaphysis, the bone cortex was thinner with decreased bone mineral as reflected by a reduction in CSA and cortical thickness. 6. Despite the thinner cortex, vBMD of the tibial diaphysis was preserved. 7. The PSSI (surrogate measure of bone strength) was significantly reduced. 8. There was a significant loss of muscle CSA in the calves of all patients; however, when examining the cortical BMC for muscle CSA, there was a significant increase compared to able-bodied controls. 9. Patients who were able to load bear (even if only in a standing frame) had significantly greater tibial trabecular vBMD, cortical CSA and improved muscle CSA than those who could not ($p<0.05$). 10. There was no association between pQCT parameters and the occurrence of fractures. 11. Fractures were femoral or tibial in six out of seven patients (86%); lower limb fractures did not occur if tibial trabecular vBMD was greater than 100 mg/cm3. 12. There was no correlation between the occurrence of fractures and load-bearing status. 13. There was a reduction in trabecular vBMD between 7.6 yr and 10.7 yr post SCI ($p<0.01$), while cortical vBMD did not change.

		14. There was no statistically significant change in BMC, cortical thickness or pSSI Z-scores. 15. Following SCI, there was a statistically significant reduction in circularity Z-score ($p<0.001$) which resulted in a change from the typically teardrop appearance of the tibia to a more circular shape. 16. Circularity Z-scores did not change over time in those individuals with serial pQCT scans and was not associated with fracture risk; those who were not mobile had significantly lower circularity Z-scores compared to those who were mobile but there was no difference between those who could load bear (i.e., stand in a standing frame) compared to those who could not.
(Castello et al., 2012) USA Pre-Post N=6	**Population:** Age: 16.6±4.4 yr; Gender: males=3, females=3; Time since injury: 3.9±3.1 yr; Level of injury: Cervical=4, Thoracic=2; Severity of injury: AIS A=3, AIS B=1, AIS C=1, AIS D=1. **Intervention:** Functional Electrical Stimulation (FES) cycling. Stimulators were placed on hamstrings, quadriceps and gluteal muscles (45-50 rpm, 250 µs, 33.3 Hz, 70-120 mA). Sessions were 30 min, 3 times/wk over 9 mo. **Outcome Measures:** Bone mineral density (BMD) measured using Dual X-ray Absorptiometry (DXA) scans.	1. A positive, non-significant, relationship was found between change in BMD and the total number of FES biking sessions from their first to last DXA scan (r_s=0.77). 2. A positive, non-significant, relationship was found between the change in BMD and the number of months using the FES cycle from their first to last DXA scan (r_s= 0.77). 3. A weakly positive, non-significant, relationship was found between the change in BMD and the average number of biking sessions per month (r_s=0.60), as well as between the change in BMD and the time from injury at the initial evaluation (r_s=0.49).
(Lauer et al., 2011) USA RCT N=28 PEDro=6	**Population:** Age: 9.6±2.4 (5-12) yr; Gender: males=17, females=11; Time since injury: 5.1±2.9 yr; Level of injury: cervical=9, thoracic=19; Severity of injury: AIS A=20, AIS B=5, AIS C=3. **Intervention:** Subjects were randomized to one of three groups: 1) *Functional Electrical Stimulation while Cycling* (FESC): 50 rpm while seated in wheelchair (pulse duration (150 ls) and frequency (33 Hz) were fixed; current amplitude (max 140 mA) increased automatically to generate sufficient force to maintain the cadence); 2) *Passive Cycling (PC)*: Passive cycling at 50 rpm; or 3) *Electrical Stimulation (ES):* contraction of bilateral hamstrings, quadriceps, and gluteal muscles, 20 min each, 33 Hz, 300us, and 100mA. Sessions were conducted for 1 hour, 3 times/wk for 6 mo. **Outcome Measures:** Hip, distal femur, and proximal tibia Bone Mineral Density (BMD).	1. Following the interventions, there were no significant increases in BMD between or within any of the groups. 2. The FESC group exhibited non-significant increases in hip, distal femur and proximal tibia BMD. 3. The PC group exhibited a non-significant increase in hip BMD but not distal femur or proximal tibia. 4. The ES group exhibited no change in hip and distal femur BMD, but a non-significant loss at the proximal tibia. 5. There were no hip BMD differences between groups with respect to time post SCI.
(Liu et al., 2008) Australia Observational N=18	**Population:** Median age: 5.3 (0.5-15.6) yr; Gender: males=9, females=9; Time since injury: 5.0±3.6 yr; Level of injury: Cervical=6, Thoracic=12; Severity of injury: complete paraplegia=13, incomplete paraplegia=1, complete tetraplegia=2, incomplete tetraplegia=2. **Intervention:** Functional Electrical Stimulation (FES) cycling. Stimulators were placed on hamstrings, quadriceps and gluteal muscles (45-50 rpm, 250 µs, 33.3 Hz, 70-120 mA). Sessions were 30 min, 3 times/wk over 9 mo.	*Total Group Data Combined, Cross-Sectionally* 1. The 10 children with a complete motor lesion had significantly lower Legs BMC, FN and Legs BMD Z-scores at baseline; with the exception of the Arms and FN, Z-scores decreased during the 1st year, and in the 2nd year Z-scores remained low but did not decrease further. 2. Children with incomplete motor lesions showed age-appropriate scans. 3. BMD Z-scores were significantly less than zero in the Legs ($p<0.001$), total body ($p=0.02$),

	Outcome Measures: Bone mineral density (BMD) and Bone Mineral Content (BMC) of the total body, lumbar vertebrae, and femoral neck (FN), Lean Tissue Mass (LTM).	L2-L4 (p=0.04), and the FN (p<0.001), but not in the Arms. 4. BMC Z-scores of the total body (p=0.002) and Legs (p<0.001) were also less than zero. 5. With increasing time post-injury, there was a decrease in total body BMD (p=0.02) and BMC Z-scores (p=0.04). 6. The three ambulant children had normal Legs BMD and BMC; when they were excluded the time-related decrease in either Legs BMD or BMC became non-significant (p=0.08) and LTM Z-score was reduced in the Legs (p<0.001) and remained stable with time. 7. Ambulant children had higher Legs LTM Z-scores; in contrast, Arms BMD and LTM Z-scores were normal and increased with time (p=0.003 and p=0.01, respectively). 8. L2–L4 BMD Z-scores were stable with time (p>0.05). 9. There were no changes seen in body fat (% and Z-scores). *Immediate group (scans <2 yr post SCI; n=13)* 10. Only Legs BMD, Legs BMC and FN Z-scores were significantly less than zero at baseline. 11. In the first year post-SCI, BMD and BMC Z-scores of the total body fell significantly and trended towards lower values in the Legs - (p=0.07; bone mass did not increase at the expected rate); there was no reduction in BMD Z-scores in the arms. 12. In the second year, there were no significant changes in BMD or BMC Z-scores for any region, suggesting an age-appropriate accrual of bone mass. 13. Legs LTM Z-score and total body BMC/LTM Z-score decreased significantly in the first year post-SCI but not during the 2nd year of follow-up; in contrast, Arms LTM Z-score increased over the 2-yr period. *Long-term group (scans >2 yr post SCI; n=5)* 14. At the first scan they had similar BMD and BMC Z-scores to the 2-yr results of the *Immediate* group (p>0.05); there was no significant change in Z-scores over the following 2 yr (age-appropriate accrual of bone mass). 15. All children had age-appropriate increases LTM in all regions.
(Johnston, Smith, et al., 2008b) USA Case Series* N=4 *Subjects were a subset from a larger RCT by (Johnston, Smith, et al., 2009)	**Population:** *Case 1:* 7 yr, female, T4-T6, ASIA A SCI at 2 yr of age; *Case 2:* 9 yr, female, C7, ASIA A SCI at 4 yr of age; *Case 3:* 7 yr, male, T3, ASIA A SCI at 3 yr of age; *Case 4:* 11 yr, male, C7, ASIA A SCI at 3 yr of age. **Intervention:** *Intervention Group:* Functional Electrical Stimulation while cycling at 50 rpm while seated in wheelchair (pulse duration (150 ls) and frequency (33 Hz) were fixed; current amplitude (max 140 mA) increased automatically to generate sufficient force	*Case 1: FES Cycling* 1. Improvements in BMD at the femoral neck, distal femur, and proximal tibia; quadriceps muscle volume; stimulated strength of the quadriceps muscles; HDL cholesterol; resting HR; peak VO_2/kg; and peak HR; however, cholesterol, LDL, and triglyceride levels and the cholesterol/HDL ratio increased compared to baseline. 2. No changes in Ashworth scores, but parents reported decreased spasticity and looser muscles.

	to maintain the cadence). *Control Group:* Passive cycling at 50 rpm. Sessions were conducted for 1 hr, 3 times/wk for 6 mo. **Outcome Measures:** Bone mineral density (BMD) of the left femoral neck, distal femur, and proximal tibia; left quadriceps muscle volume; electrically stimulated strength of the left quadriceps; quadriceps and hamstrings muscles Ashworth scale scores; fasting lipid profile via high density lipoprotein (HDL) and low-density lipoprotein (LDL); heart rate (HR); and oxygen consumption (VO_2/kg).	*Case 2: FES Cycling* 3. Improvements in BMD at the femoral neck, distal femur, and proximal tibia; quadriceps muscle volume; stimulated quadriceps muscle strength; and hamstring muscle spasticity; however, cholesterol, LDL, HDL, and triglyceride levels and the cholesterol/HDL ratio worsened as compared to baseline. 4. The parents reported bigger, firmer muscles; decreased bowel program completion times; increased appetite; and increased spasticity that did not require medical intervention. *Case 3: Passive Cycling* 5. Improvements in femoral neck BMD, hamstring spasticity, and triglyceride levels. 6. Distal femur and proximal tibia BMD and stimulated quadriceps strength were lower as compared to baseline, and LDL levels and the cholesterol/HDL ratio were elevated. 1. Parents reported decreased bowel accidents and new sensation in his knees and stomach. *Case 4: Passive Cycling* 2. Improvements in BMD at the femoral neck, distal femur, and proximal tibia; quadriceps muscle volume; stimulated quadriceps strength; hamstring spasticity; cholesterol; LDL cholesterol; resting HR; and peak VO_2/kg. 3. HDL cholesterol decreased as compared to baseline but the cholesterol/HDL ratio was unchanged. 4. Parents reported decreased spasticity, looser muscles, increased energy, decreased lower extremity swelling, and increased appetite.
(Lauer et al., 2007) USA Observational N=28	**Population:** Age: 9.6±2.5 yr; Gender: males=17, females=11; Time since injury: 4.5±2.9 yr; Level of injury: Cervical=8, Thoracic=20; Severity of injury: AIS A=25, AIS B=3. **Intervention:** None. **Outcome Measures:** Bone mineral density (BMD) of the left hip, distal femur, and proximal tibia.	1. For the group as a whole, BMD values at the hip were 0.48±0.17 g/cm², 0.41±0.17 g/cm², and 0.47±0.17 g/cm² for femoral neck, greater trochanter, and Ward's triangle, respectively. 2. Total hip BMD was 0.48±0.17 g/cm². 3. At the knee, BMD values were 0.38±0.10 and 0.37±0.07 g/cm² for the distal femur and proximal tibia, respectively. 4. In the regions where the Z-scores could be calculated, overall BMDs were 64.4%, 64.2%, and 57.8% of age- and sex-matched normative values for the femoral neck, greater trochanter, and Ward's triangle, respectively. **Given the large variations and small sample size, no statistical tests were performed.
(Kannisto et al., 1998) Finland Observational N=35	**Population:** *Pediatric-onset SCI:* Median age at interview: 31 (18-63) yr; Median age at injury: 12.9 (0-17.1) yr; Gender: males=25, females=10; Median time since injury: 19 (1.5-57) yr; Level of injury: complete paraplegia=24, incomplete paraplegia=3, complete tetraplegia=3, incomplete tetraplegia=5. **Intervention:** None. Densitometry and laboratory assays. **Outcome Measures:** Bone Mineral Density (BMD) of lumbar spine, proximal femur and regional sites (femoral neck, trochanteric area, intertrochanteric area,	1. BMD levels were within the normal range in the lumbar spine; mean BMD at the lumbar spine was 1.08±0.17 g/cm² which represents 99.5% of the age and sex adjusted mean (Z-score) and 70.04 SD of peak bone mass measured in 30-yr old persons of the same gender as the patients (T- score). 2. At the hips, accurate subtraction between bone and soft tissues with the densitometer failed in seven out of the 34 patients. 3. BMD at the proximal femur was on an average 0.72±0.23 g/cm² which is 72.05 SD of the age and gender adjusted mean value (Z-

	Ward's triangle), presence of osteoporosis (decrease of more than 2.5 SD compared to peak bone density reference data), urinary calcium, phosphate and creatinine, Alkaline Phosphatase (AP), Bone isoenzyme (BAP), Osteocalcin (OC) assay, urinary Hydroxyproline (HYP) and deoxypyridinoline (DPD).	score); mean T-score was 72.61 which represents established osteoporosis. 4. BMD in the femoral neck was 0.69±0.19 g/cm^2. 5. BMD in Ward's triangle was 0.60±0.24 g/cm^2. 6. Lowest measurements were at the intertrochanteric level where mean BMD was 0.52 g/cm^2. 7. At the lumbar spine 10/29 of the patients had a T-score which was under 71 SD and 3/29 of the patients had T-scores less than 72 SD; none of the patients had a T-score less than 72.5 SD at the lumbar spine. 8. At the femoral neck 21/27 of the patients had T-scores under 71 SD, 19/27 had T-scores less than 72 SD and 16/27 had a T-score less than 72.5 SD. 9. The dissociation between axial and peripheral BMD (lumbar spine versus total femoral area) was significant (p<0.001). 10. Though statistically significant (p=0.04), there was no clinical difference in BMD between those with tetraplegia or paraplegia at the lumbar level. 11. There was no statistically significant difference in hip BMD between those with paraplegia versus tetraplegia. 12. In comparing individuals with lesions at C1±T6 to those with lesions ≤T7, there were significant differences in BMD at lumbar (p=0.004) and hip (p<0.01) with those sustaining higher injuries having lower BMD. 13. Regression showed BMD of the proximal femur (b=0.49, p<0.01) and the femoral neck (b=0.57, p<0.01) was correlated with bodyweight but not body height, age at the time of injury, age at the time of examination or to the time elapsed since injury. 14. Biochemical markers of bone metabolism showed no signs of still ongoing accelerated bone formation or resorption.
(Moynahan, Betz, et al., 1996) USA Observational N=51	**Population:** Age: 14.5±4.2 (3-20) yr; Gender: males=30, females=21; Level of injury: cervical=19, thoracic/lumbar=32. **Intervention:** None. Densitometry and laboratory assays. **Outcome Measures:** Bone Mineral Density (BMD) of femoral neck, Ward's triangle and intertrochanteric region of the hip, presence of spasticity, number of pathological fractures.	1. Baseline measurements at the femoral neck, Ward's Triangle and intertrochanteric region were normalized by sex and age and then averaged; there was a trend toward lower BMD at the hip in SCI subjects as compared with their non-disabled peers: femoral neck=64.2±17.6%, Ward's Triangle=64.4±17.6% and intertrochanteric region=55.9±16.0%. 2. In total, 10 subjects had one or more pathological fractures of the leg. 3. Normalized BMD were compared to non-fracture SCI subjects and there was a trend toward lower BMD in subjects with fractures (p<0.05); the upper limit of the fracture group (the value above which no subject showed a fracture) was 87 percent for the femoral neck, 90 percent for Ward's Triangle and 65 percent for the intertrochanteric region. 4. At only the intertrochanteric region, those with tetraplegia had lower BMD than those with paraplegia (p<0.05). 5. In total, 46 subjects had spastic legs and 5 subjects had flaccid legs. 6. Subjects with spasticity generally showed higher bone densities than those without

		spasticity at the femoral neck and Ward's triangle (p<0.05 for both) but not the intertrochanteric region (analysis lacked statistical power).
Heterotopic Ossification		
(Vogel et al., 2002b) *Part II* USA Observational N=216	**Population:** Age at injury: 14.1±4.0 yr; Age at interview: 28.6±3.4 yr; Gender: males=150, females=66; Time since injury: 14.2±4.6 yr; Level of injury: tetraplegia=123, paraplegia=93. Severity of injury: C1-4 ABC=41, C5-8 ABC=67, T1-S5 ABC=82, tetra/para D=26. **Intervention:** None. Survey. **Outcome Measures:** Prevalence of heterotopic ossification.	1. Heterotopic ossification was reported by only 24 subjects. Heterotopic ossification was more common in those with more severe injuries (C1-4 A-B-C) (23%), compared to the other injury severity groups (9%) (p=0.013).
(Garland et al., 1989) USA Observational N=152	**Population:** Heterotopic Ossification Group: Age: 8.5 yr (3 mo-15 yr); Gender: males=12, females=3; Injury etiology: trauma=11, vascular compromise=2, infection=1, progressive kyphosis=1. Level and severity of injury: thoracic complete=13, cervical incomplete=2. **Intervention:** None. Chart Review. **Outcome Measures:** Heterotopic Ossification (HO) incidence location, signs and symptoms, incidence of pressure ulcers, hip dislocations, alkaline phosphatase levels, surgical treatment.	1. Among 152 individuals, 15 developed HO (9.9%). 2. There were 19 different HO locations, most commonly the hip. 3. Three ossification patterns of the hip were identified: anterior, abductor muscle region, and inferomedial. 4. The femur was the only area of non-joint HO formation. 5. Two patients had HO at two joints and one patient had HO at three joints. 6. Average time from spinal insult to diagnosis of HO was 6 yr 5mo (2 mo-19 yr); considering only neurogenic HO, the average time was 14 mo (3-36 mo). 7. Most common sign of HO was a reduction in joint motion. 8. At the hip, 11 patients had pressure ulcers. 9. At the hip, 3 patients had dislocations, two of which had pressure ulcers as well. 10. When HO was detected, eight patients had alkaline phosphatase levels obtained of which they were elevated in five (3 primary, 2 secondary). 11. Three patients had resorption of HO of at least one grade. 7. Five patients were treated with surgery at the hip (mean 3.2 surgeries) for wound debridement, resection of HO, etc.
Hypercalcemia		
(Massagli & Cardenas, 1999) USA Case Series N=9	**Population:** Age: 0-18 yr=3, 19-25 yr=4, 26-41 yr=2; Gender: males=7, females=2; Level of injury: C1-4=1, C5-7=6, T1-12=1; Severity of injury: AIS A=6, AIS B=1, AIS C=1, AIS D=1. **Intervention:** 60 mg pamidronate. **Outcome Measures:** Calcium levels.	1. Hypercalcemia onset occurred 3-16 weeks post injury with typical symptoms including nausea. 2. Ionized calcium levels at the time of treatment ranged from 1.29 to 1.53 mmol/L and the corrected serum calcium was 12.7 mg/dL. 3. Original 60 mg pamidronate dose sufficiently treated seven of nine patients; the remaining two required additional doses. 4. One patient experienced transient drug-related fever. 5. For four patients, the serum or ionized calcium level decreased to the hypocalcemic range after treatment, but they were asymptomatic.