Prävention der Osteoporose und therapeutische Konzepte von Knochenerkrankungen im Kindes- und Jugendalter

Prof.Dr.Eckhard Schönau

Klinik und Poliklinik für Kinder und Jugendliche

Universitäts-Klinikum Köln

- 1. Alltagsbeobachtungen
- 2. Muskel und Skelett – eine funktionelle Einheit
- 3. Störungen der Skelettentwicklung
- 4. Das „Peak-Bone-Mass-Konzept“

Überlassen von Prof. Koebke

NEUGEBORENES MIT SMA

Smit TH et al., J Bone Miner Res 2002

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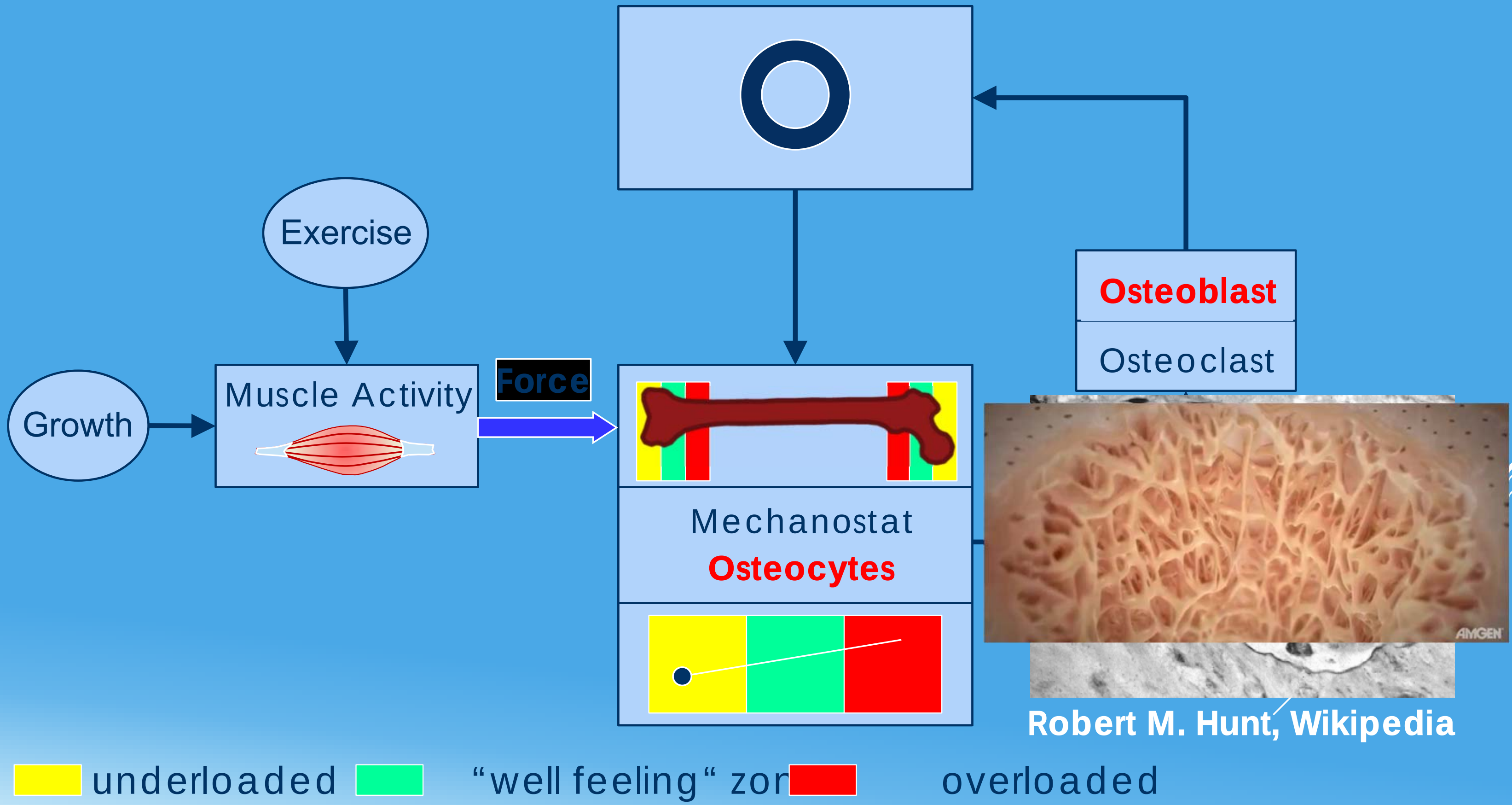
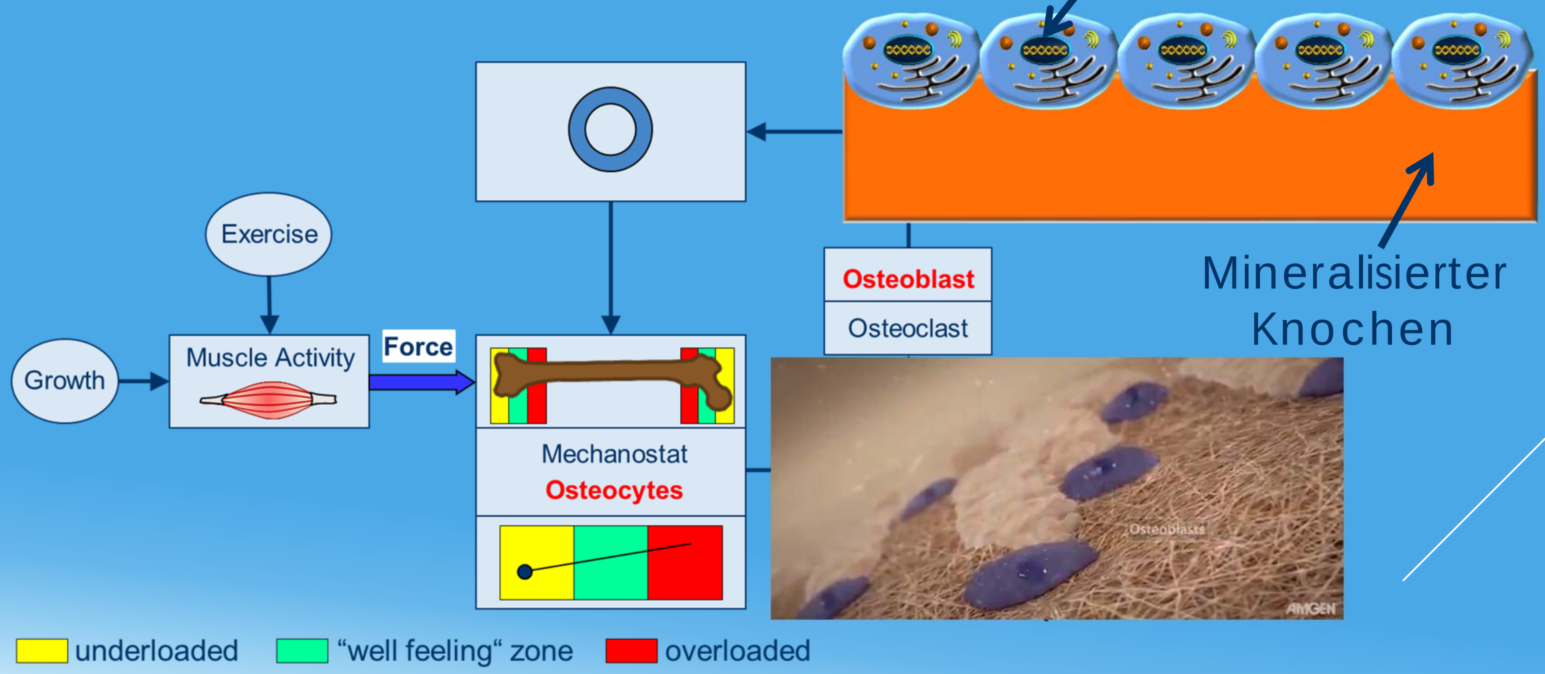
Mechanostat



Mechanostat

Schritt 1: Osteoidsynthese

Neu synthetisierte Knochenmatrix

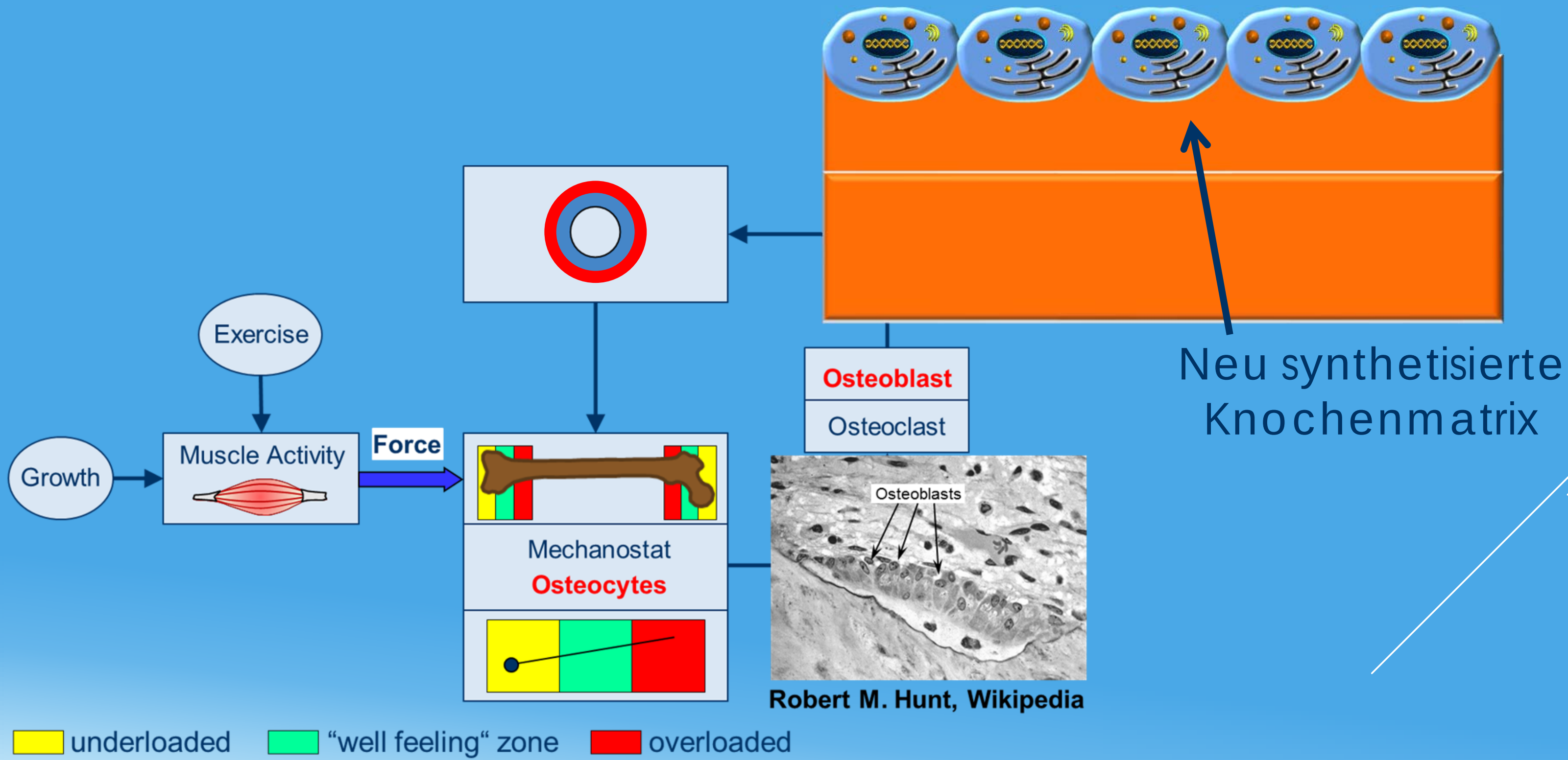


Mineralisierter Knochen

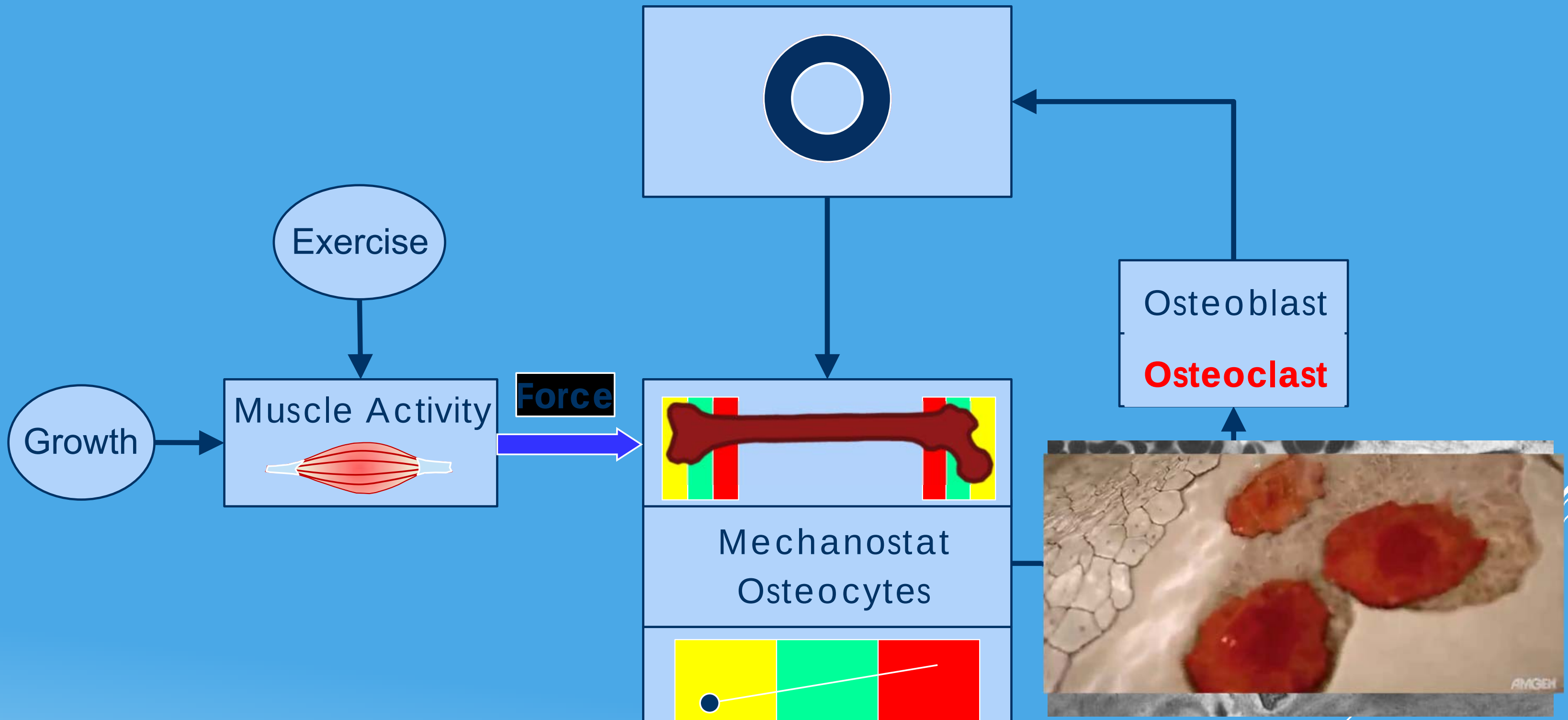
Mechanostat

Ca^{2+} PO_4 Ca^{2+} PO_4 Ca^{2+} PO_4

Schritt 2: Mineralisation



Mechanostat

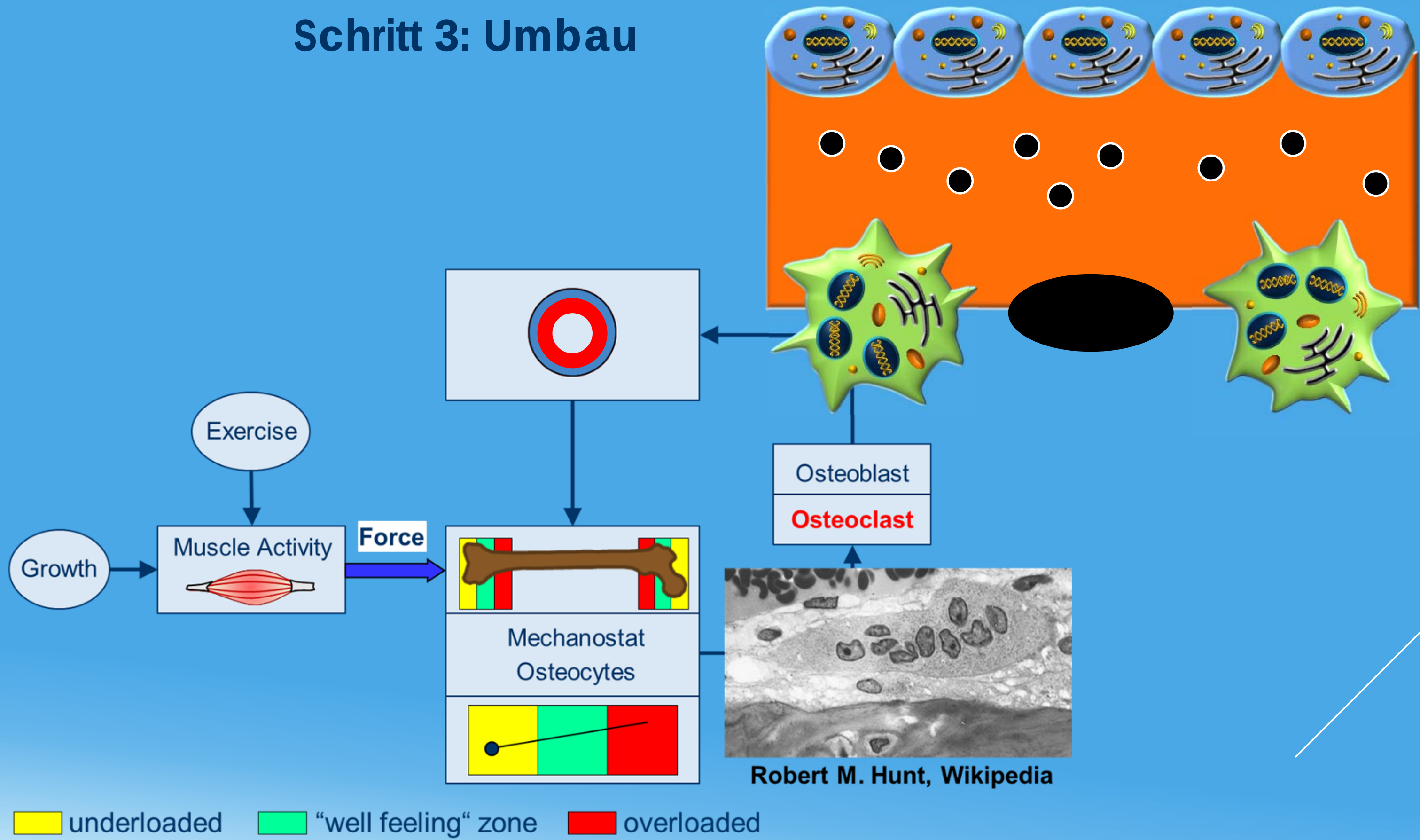


Robert M. Hunt, Wikipedia

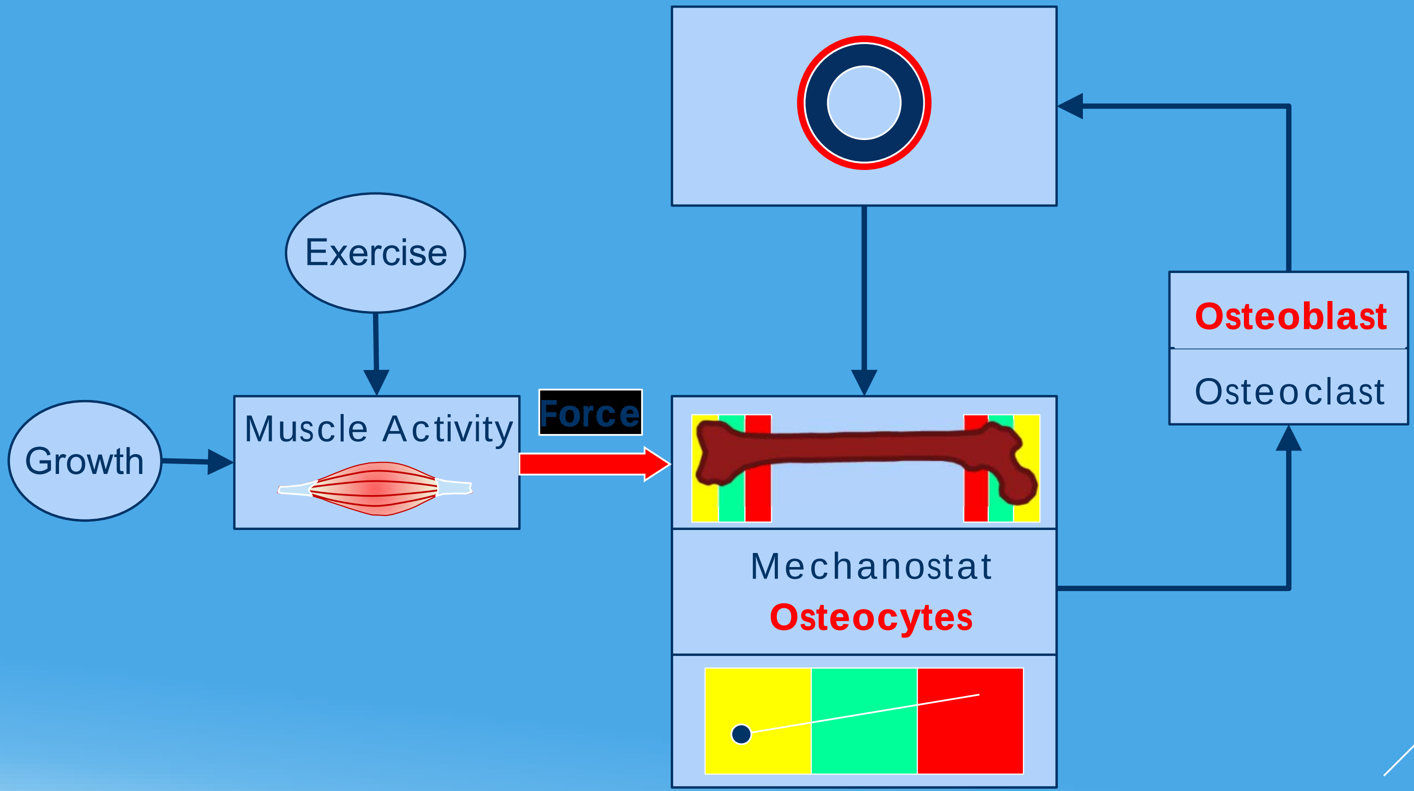
underloaded “well feeling“ zone overloaded

Mechanostat

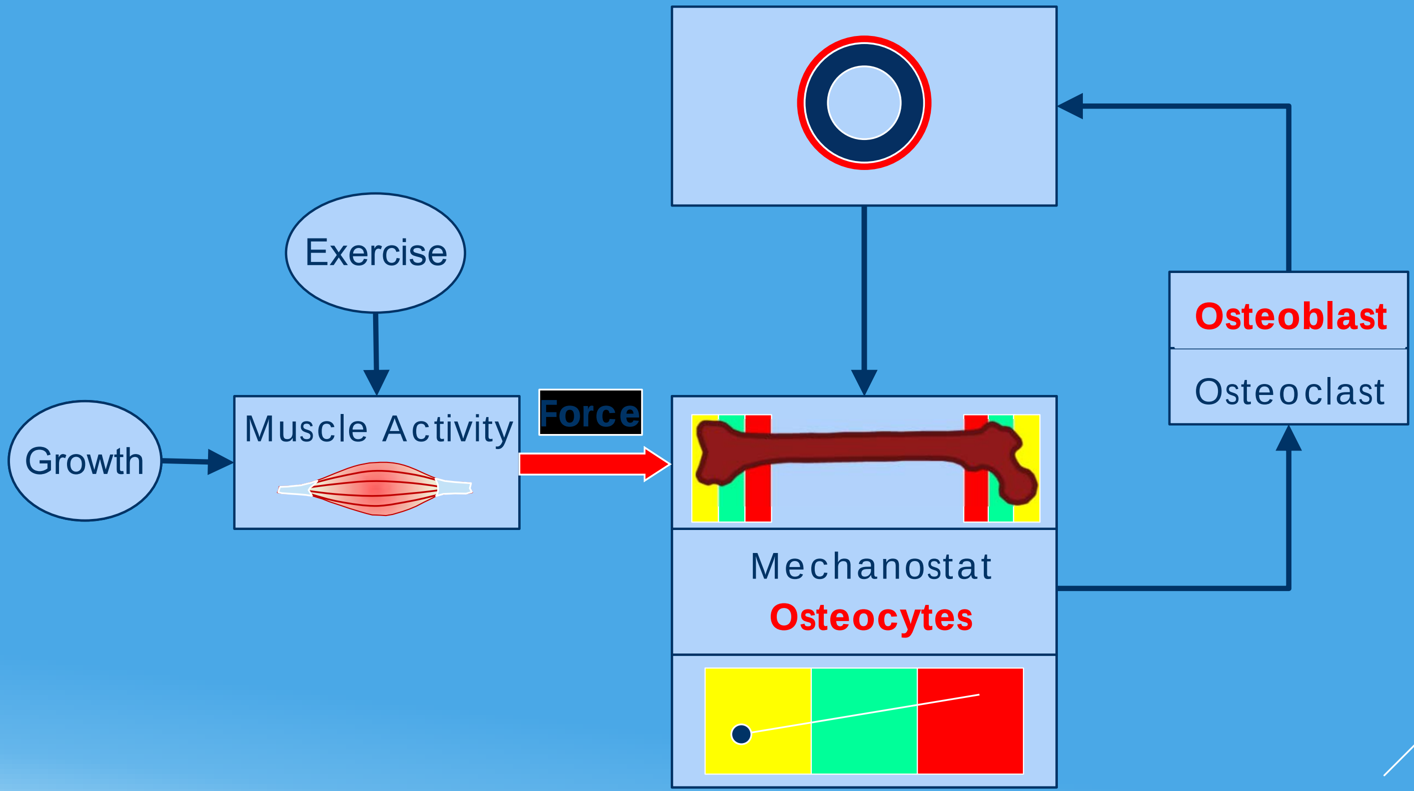
Schritt 3: Umbau



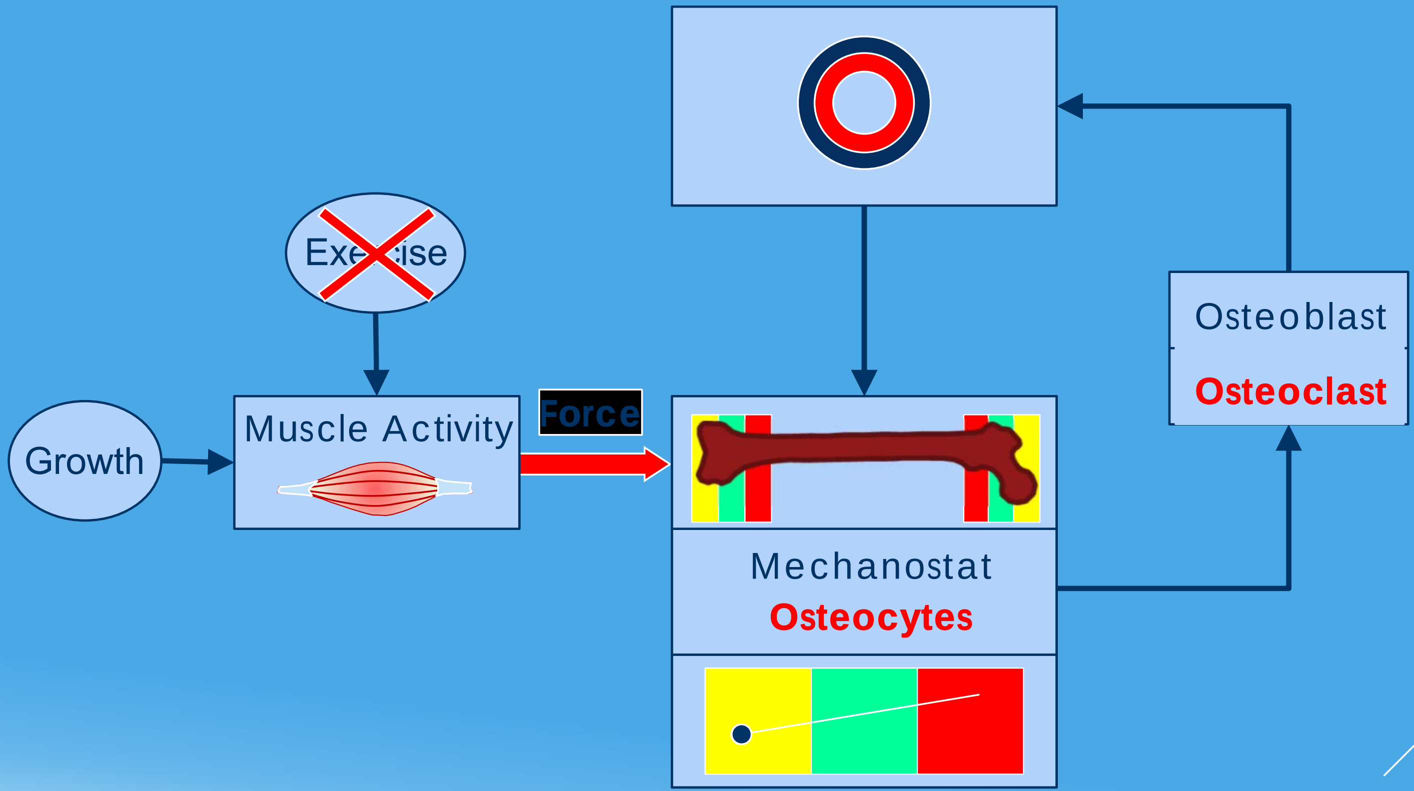
Physiology during Growth



Exercise


Exercise
Growth
Muscle Activity
Force
Mechanostat
Osteocytes
Osteoblast
Osteoclast

Inactivity



~~Exercise~~
Growth
Muscle Activity
Force
Mechanostat
Osteocytes
Osteoblast
Osteoclast

The Journal of Clinical Investigation

2017

COMMENTARY

The brains of the bones: how osteocytes use WNT1 to control bone formation

Frank Rauch

Shriners Hospital for Children and McGill University, Montreal, Quebec, Canada.

WNT proteins drive the development and maintenance of many tissues, including bone. It is less clear which of the many WNT proteins act on bone or where these WNTs act in the skeleton; however, loss-of-function mutations in *WNT1* cause bone fragility in children and adults. In this issue of the *JCI*, Joeng and colleagues demonstrate that bone formation is under the control of WNT1 produced by osteocytes, the cells that reside deep in the bone matrix and form dendritic networks. The implication of WNT1 in the control of bone formation identifies a potential new target for the treatment of low bone mass disorders, such as osteoporosis.

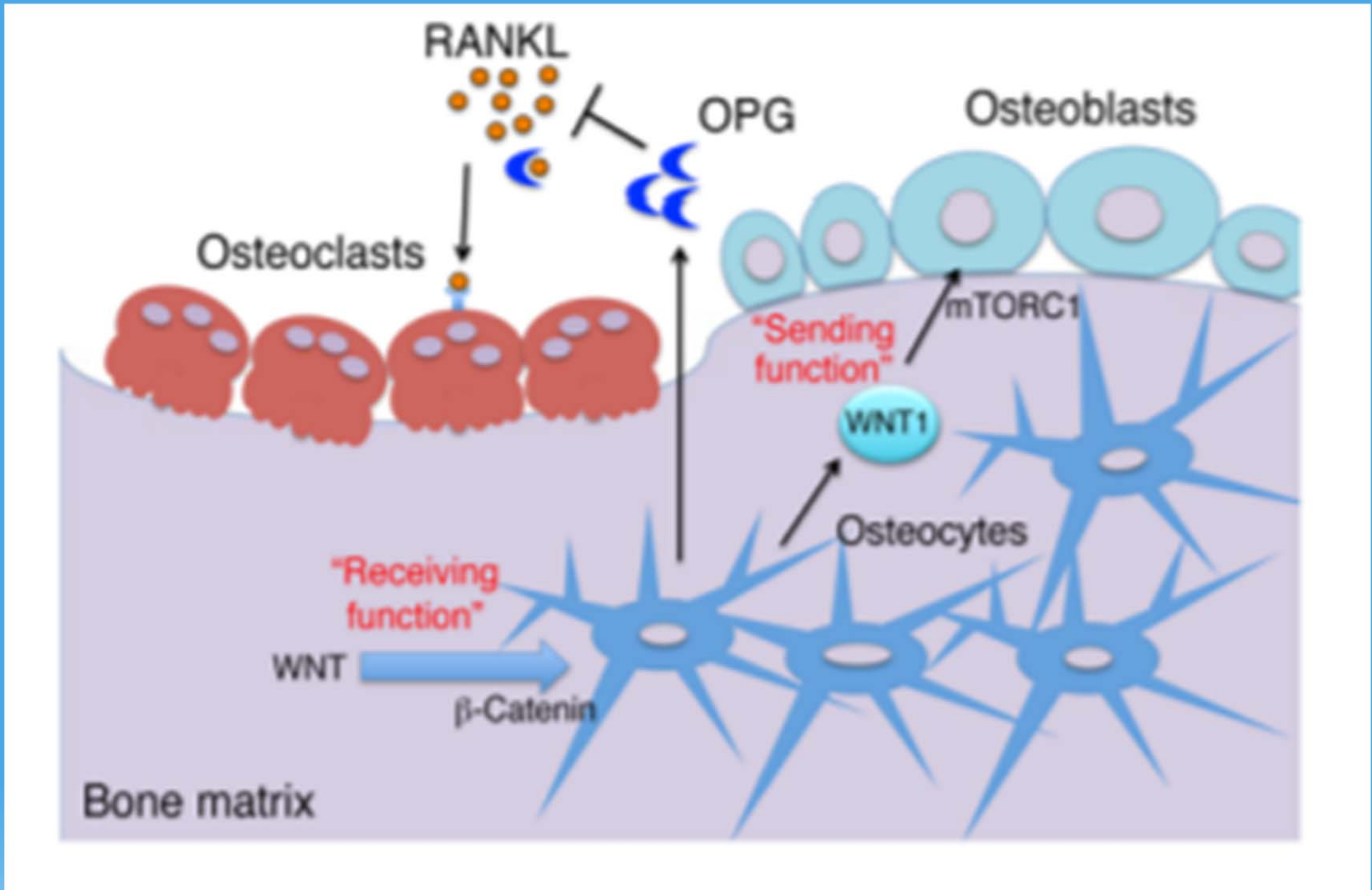
Which WNT, where?

WNT1 mutations have been reported to

in the biological adaptation of bones to mechanical stimuli (7). More generally, the osteocyte system is ideally positioned for integrating input from local and systemic factors and for orchestrating teams of effector cells (osteoblasts and osteoclasts) that are recruited to carry out the resulting action plan.

WNT1 in osteocytes

In this issue, Joeng et al. set out to explore the mechanism whereby WNT1 determines bone mass (9). Previous observations from this group established that global loss of WNT1 causes low bone mass and



JOENG KS 2017 J CLIN INVESTIGATION

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- 4. Das „Peak-Bone-Mass-Konzept“

Störung der Knochengesundheit

Störung der Knochengesundheit

Grundgerüst
Struktur

Störung der Knochengesundheit

Grundgerüst
Struktur

Mineralisation
Härte

Störung der Knochengesundheit

Grundgerüst
Struktur

Mineralisation
Härte

Festigkeit

Störung der Knochengesundheit

Grundgerüst
Struktur

Mineralisation
Härte

Festigkeit

Fraktur

Störung der Knochengesundheit

Grundgerüst
Struktur

Mineralisation
Härte

Störungen:

Störungen:

Festigkeit

Fraktur

Störung der Knochengesundheit

Grundgerüst
Struktur

Mineralisation
Härte

Störungen:

- Genetik:
  OI
- Stimulation:
  Inaktivität
- Chron. Erkrankungen:
  M. Crohn
- Medikamente:
  Kortison
- Hormone
  GH- /Östrogen-Mangel

Festigkeit

Fraktur

Störungen:

Abb. 13.15 Babygramm eines Säuglings mit Osteogenesis imperfecta Typ II nach Sillence (freundlicherweise überlassen von PD Dr. Brenner, Univ.-Kinderklinik Bonn).

Störung der Knochengesundheit

Grundgerüst Struktur

Störungen:

- Genetik:
  OI
- Stimulation:
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- Chron. Erkrankungen:
  M. Crohn
- Medikamente:
  Kortison
- Hormone
  GH- /Östrogen-Mangel

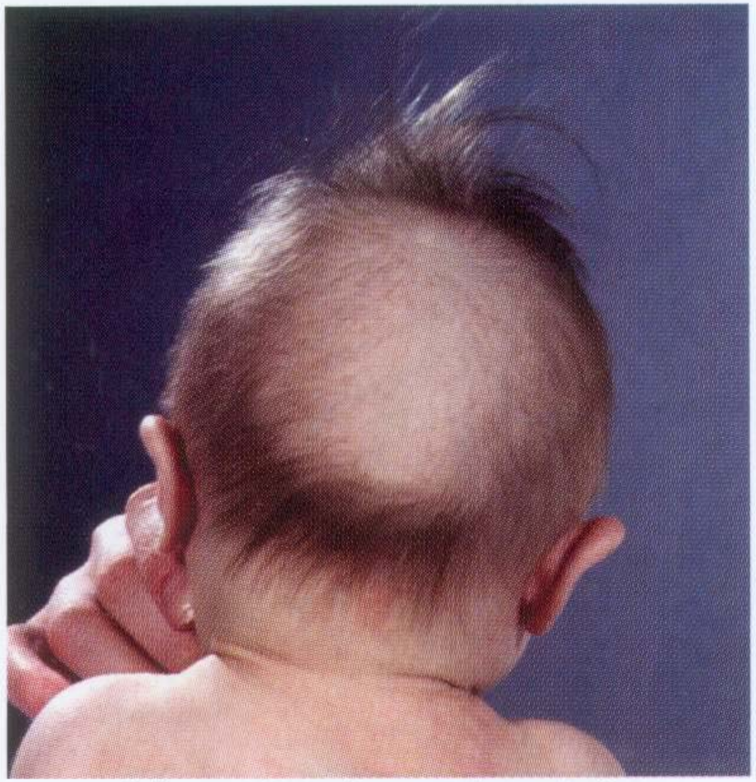
Festigkeit

Fraktur

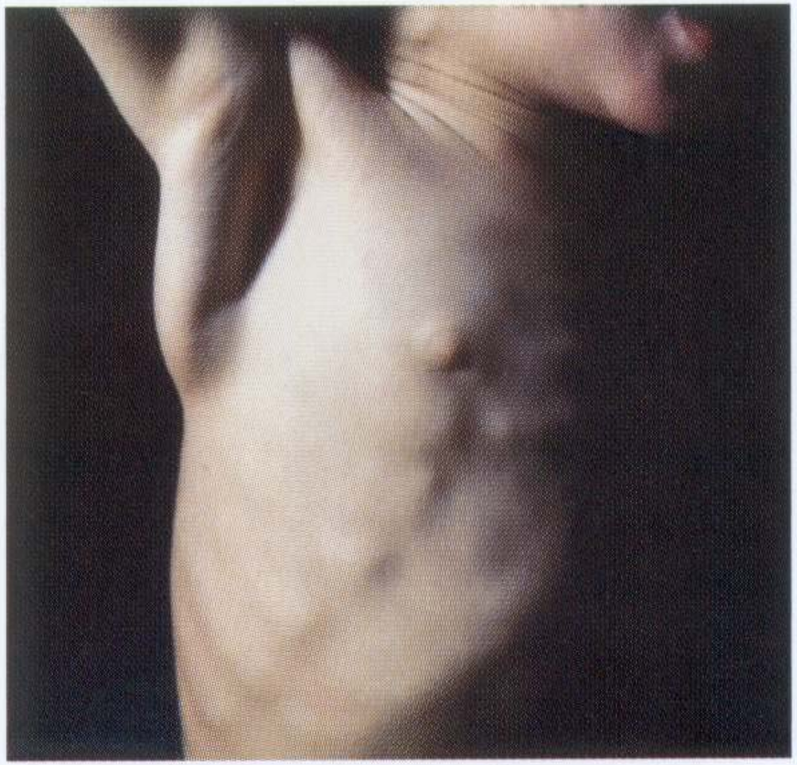
Mineralisation Härte

Störungen:

- Genetik:
  Vit. D Mangel
  Phosphatverlust
  Alkalische Phosphatase
- Substratmangel:
  Ernährung
  Resorption (Darm)
  Calcium / Phosphat
- Hormone
  PTH / Vitamin D



Ausgedehnte Hinterhauptglatze bei Rachitis.



Rachitischer Rosenkranz (oft erst später auftretend).

T. Baumann 2002

Störung der Knochengesundheit

Grundgerüst Struktur

Störungen:

- Genetik:
  OI
- Stimulation:
  Inaktivität
- Chron. Erkrankungen:
  M. Crohn
- Medikamente:
  Kortison
- Hormone
  GH- /Östrogen-Mangel

Festigkeit

Fraktur

Sturzrisiko

Mineralisation Härte

Störungen:

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  Vit. D Mangel
  Phosphatverlust
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- Substratmangel:
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  Resorption (Darm)
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Therapeutische Prinzipien

Therapeutische Prinzipien

Kein Aufbau

Störung Struktur

Verlust

Therapeutische Prinzipien

Kein Aufbau

Störung Struktur

Verlust

Calcium ↓

Störung Mineralisation

Phosphat ↓

Therapeutische Prinzipien

Muskelaufbau
Parathormon

↓

Kein Aufbau

Störung Struktur

Verlust

Calcium ↓

Störung Mineralisation

Phosphat ↓

Therapeutische Prinzipien

Muskelaufbau
Parathormon

↓

Kein Aufbau

Störung Struktur

Verlust

↑

Bisphosphonate

Calcium ↓

Störung Mineralisation

Phosphat ↓

Therapeutische Prinzipien

Muskelaufbau
Parathormon

Kein Aufbau

Störung Struktur

Verlust

Bisphosphonate

Calcium
Vitamin D

Calcium ↓

Störung Mineralisation

Phosphat ↓

Therapeutische Prinzipien

Muskelaufbau
Parathormon

Kein Aufbau
Störung Struktur
Verlust

Bisphosphonate

Calcium
Vitamin D

Calcium ↓
Störung Mineralisation
Phosphat ↓

Phosphat
AK-FGF-23

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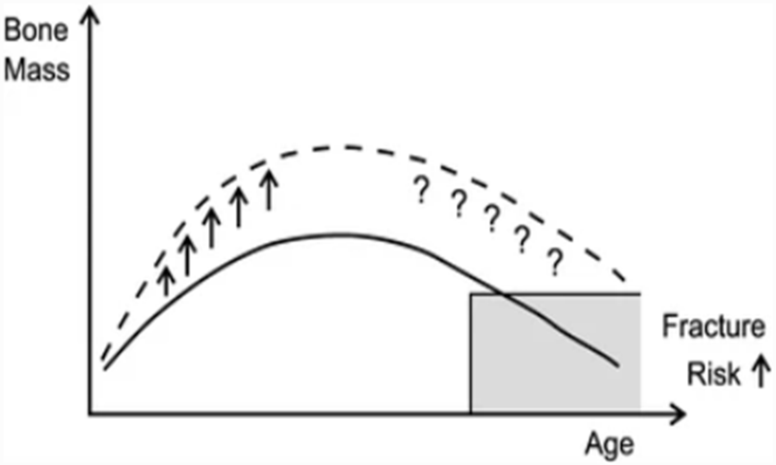
The peak bone mass concept: is it still relevant?

Eckhard Schönau

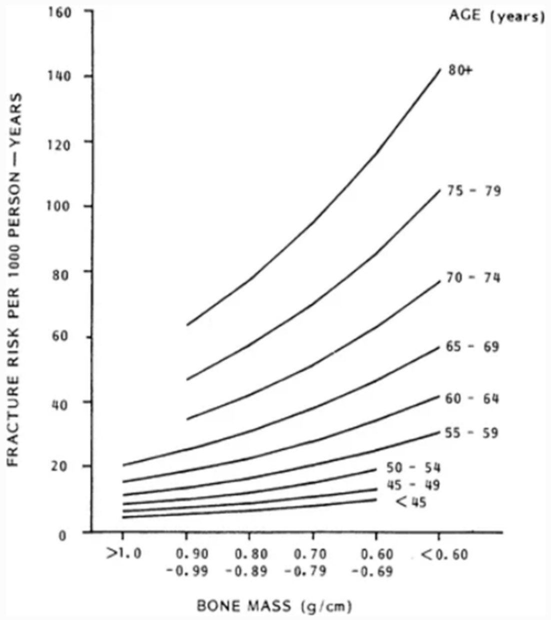
Pediatric Nephrology **19**, 825–831 (2004) | Cite this article

Fig. 1



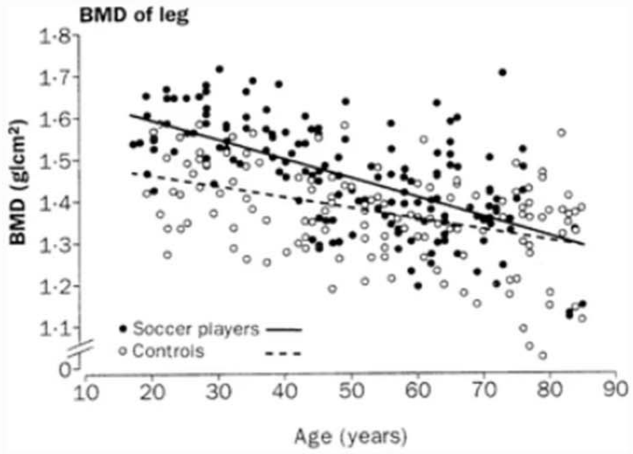
Peak bone mass concept: fracture prevention by improvement of individual bone mass during childhood and adolescence?

Fig. 5



Relationship between bone mass and age and fracture risk. Reproduced with permission from [34]

Fig. 6



Bone mineral density (*BMD*) in active and retired soccer players compared with controls. Reproduced with permission from [41]

Fig. 4

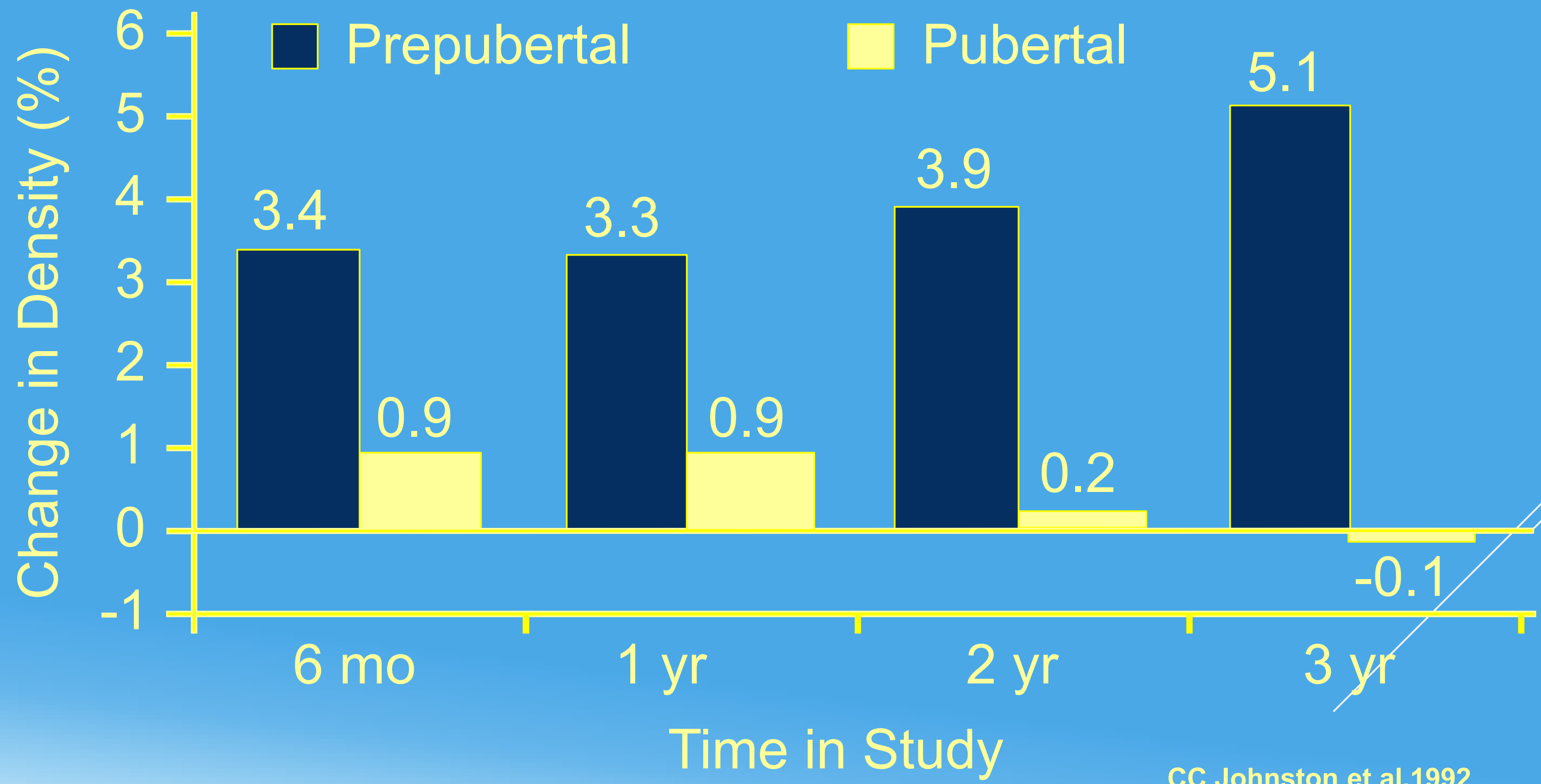
"... I have sketched a bone whose natural length has been increased three times and whose thickness has been multiplied until, for a correspondingly large animal, it would perform the same function which this small bone performs for its small animal." From Galileo Galilei [50]

The peak bone mass concept: is it still relevant?

Eckhard Schönau

Pediatric Nephrology **19**, 825–831 (2004) | Cite this article

CALCIUM SUPPLEMENTATION AND INCREASES IN BONE MINERAL DENSITY IN CHILDREN



CC Johnston et al.1992

Table 1. Differences in BMD[1] and Markers[2] of Skeletal Turnover (Supplemented-Placebo)

	Year 3	*Year 5*	*Year 6*
Radius			
prepubertal	+5.1%*	+2.9%	0.5% (−3.5, +4.5%)
peripubertal	−0.1%	+0.2%	−1.0% (−3.9, +1.9%)
Spine L2–L4			
prepubertal	+2.8%*	+1.5%	+1.7% (−0.9, +4.3%)
peripubertal	−1.0%	−0.6%	−1.8% (−4.7, +0.9%)
Femoral neck			
prepubertal	+1.2%	0.0%	−0.3% (−4.7, +4.1%)
peripubertal	−0.4%	−1.1%	+0.6% (−2.4, +3.5%)
Trochanter			
prepubertal	+3.5%*	+1.5%	+2.6% (−1.2, +6.3%)
peripubertal	+0.2%	+1.0%	+1.1% (−3.9, +6.0%)
Osteocalcin			
prepubertal	−15.1%*	−4.0%	+0.9% (−3.1, +4.9%)
peripubertal	−3.0%	+4.8%	+17.1% (−0.3, +34.5%)
TRAP			
prepubertal	−5.7%	+2.5%	+0.6% (−3.3, +4.6%)
peripubertal	−3.9%	+1.7%	−2.5% (−11.3, +6.3%)

[1]Differences in BMD are expressed as percent gain in BMD for calcium minus percent gain placebo from baseline to year 3, year 5, and year 6.

[2]Differences in markers are the within-pair differences at stated time points expressed as a percent.

*$p < 0.05$, supplemented vs. placebo.

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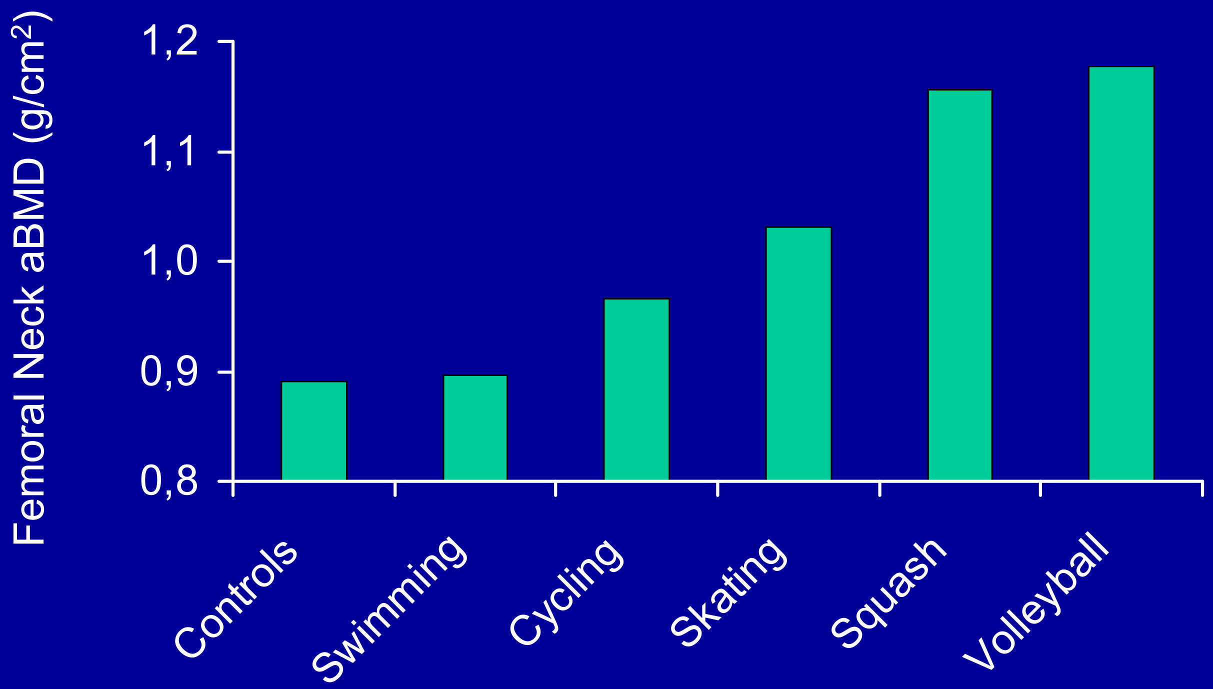
Hip Bone Density in Premenopausal Athletes

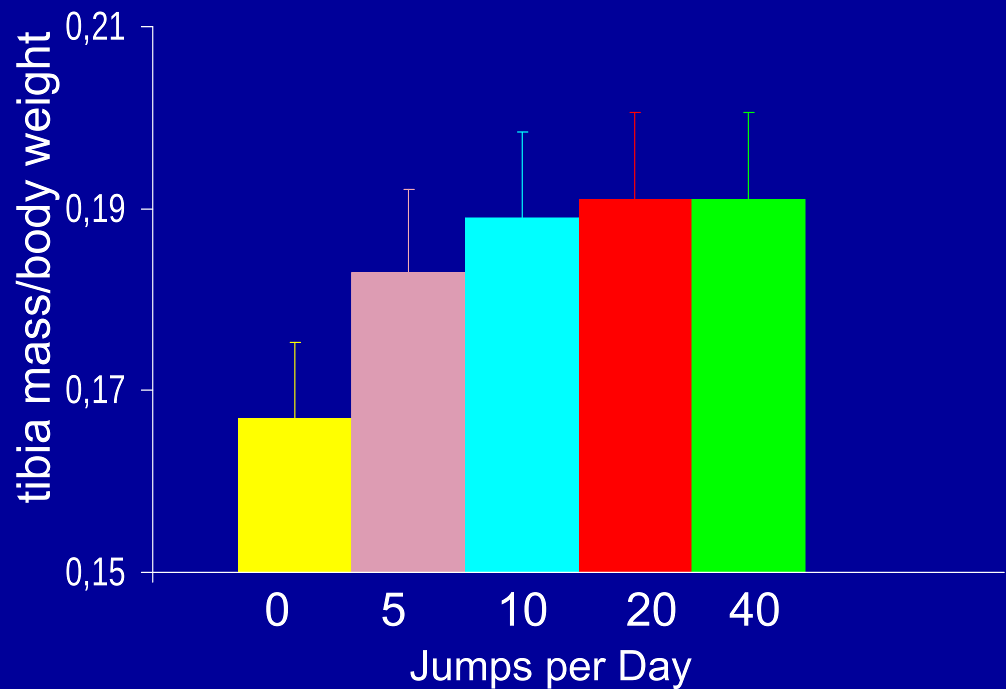


- High-impact sports have more effect on bone than low-impact sports

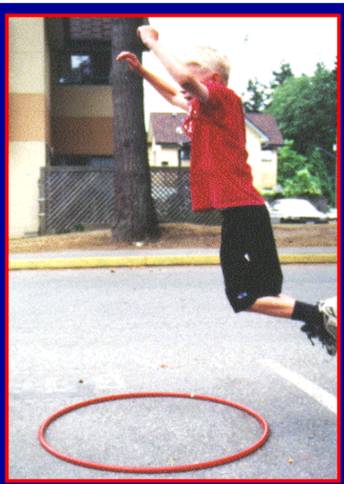
Nikander et al, *J Bone Miner Res* 2005;20:520

Characteristics of Osteogenic Activity

- 8-week study in young female rats
- Jumping to a height of 40 cm

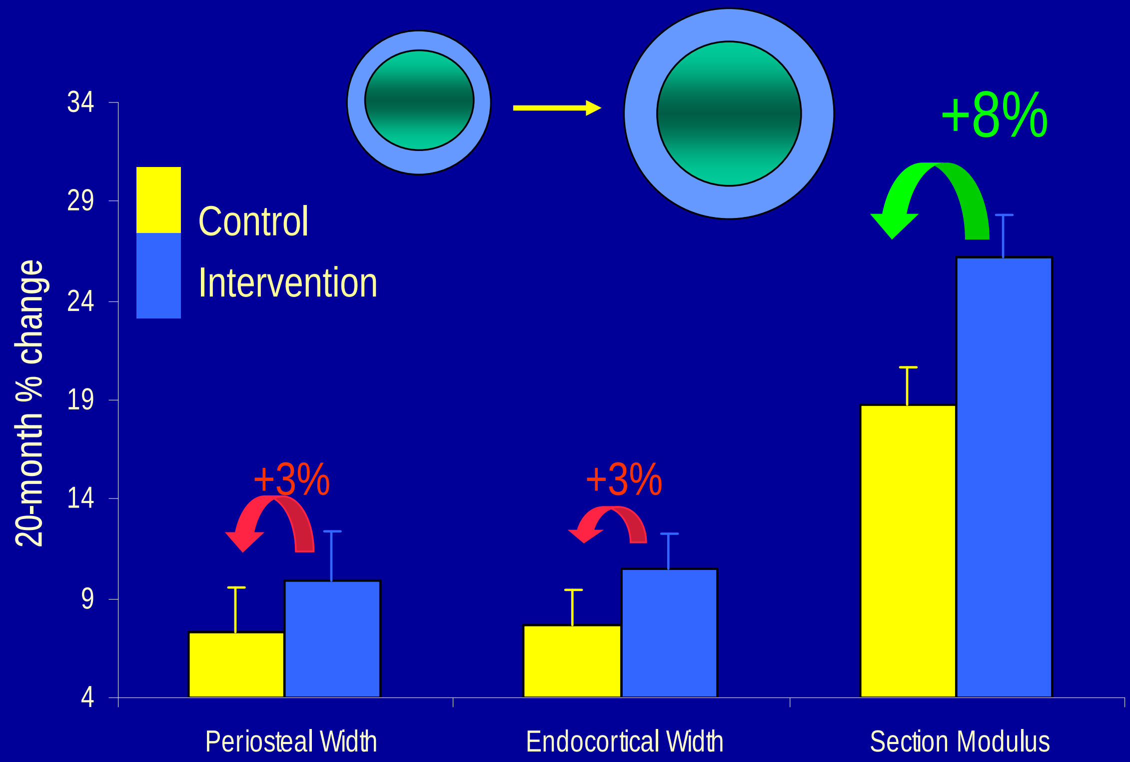


Umemura et al, *J Bone Miner Res* 1997;12:1480



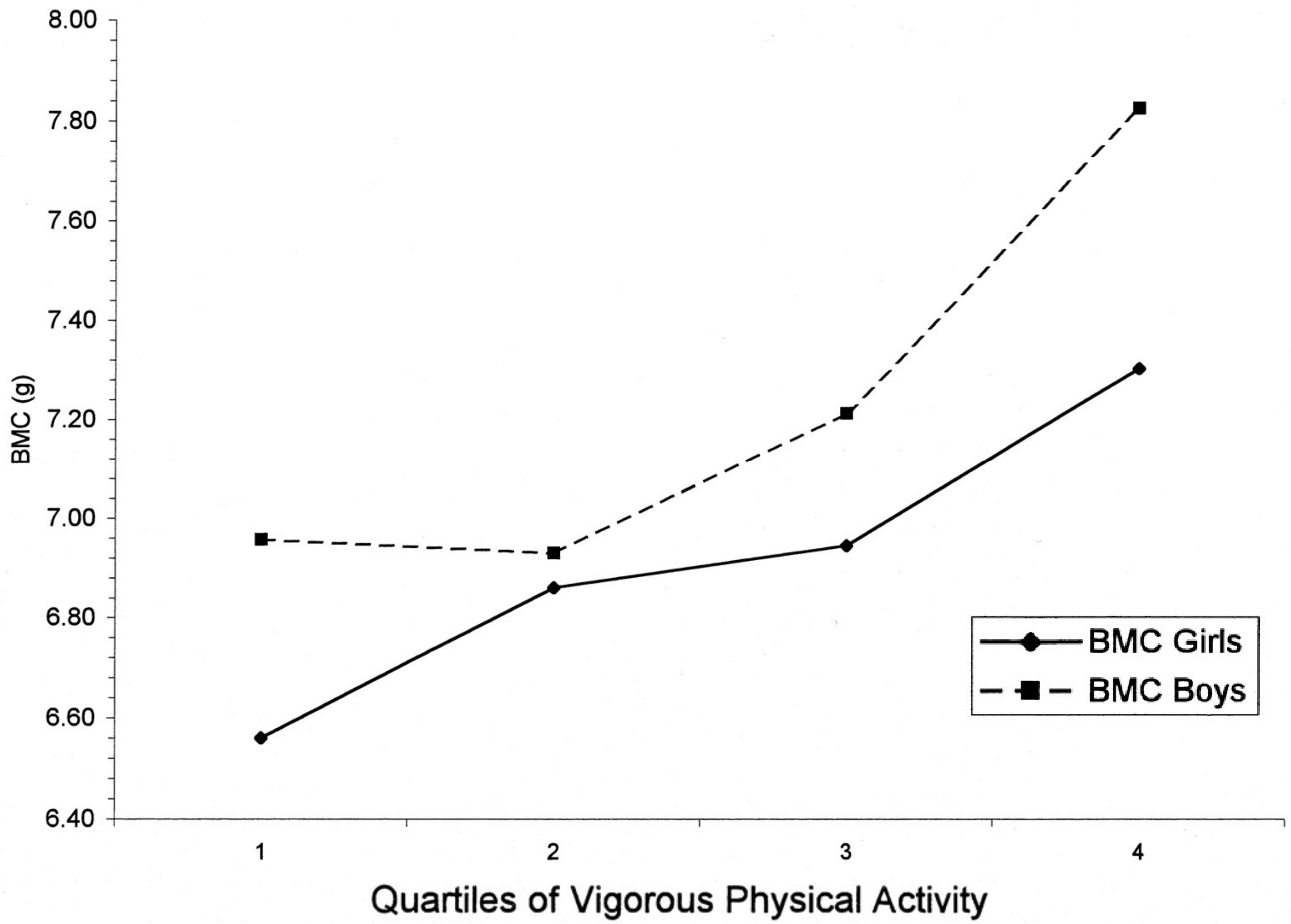
Effect of Jumping

Hip Structure Analysis in Boys



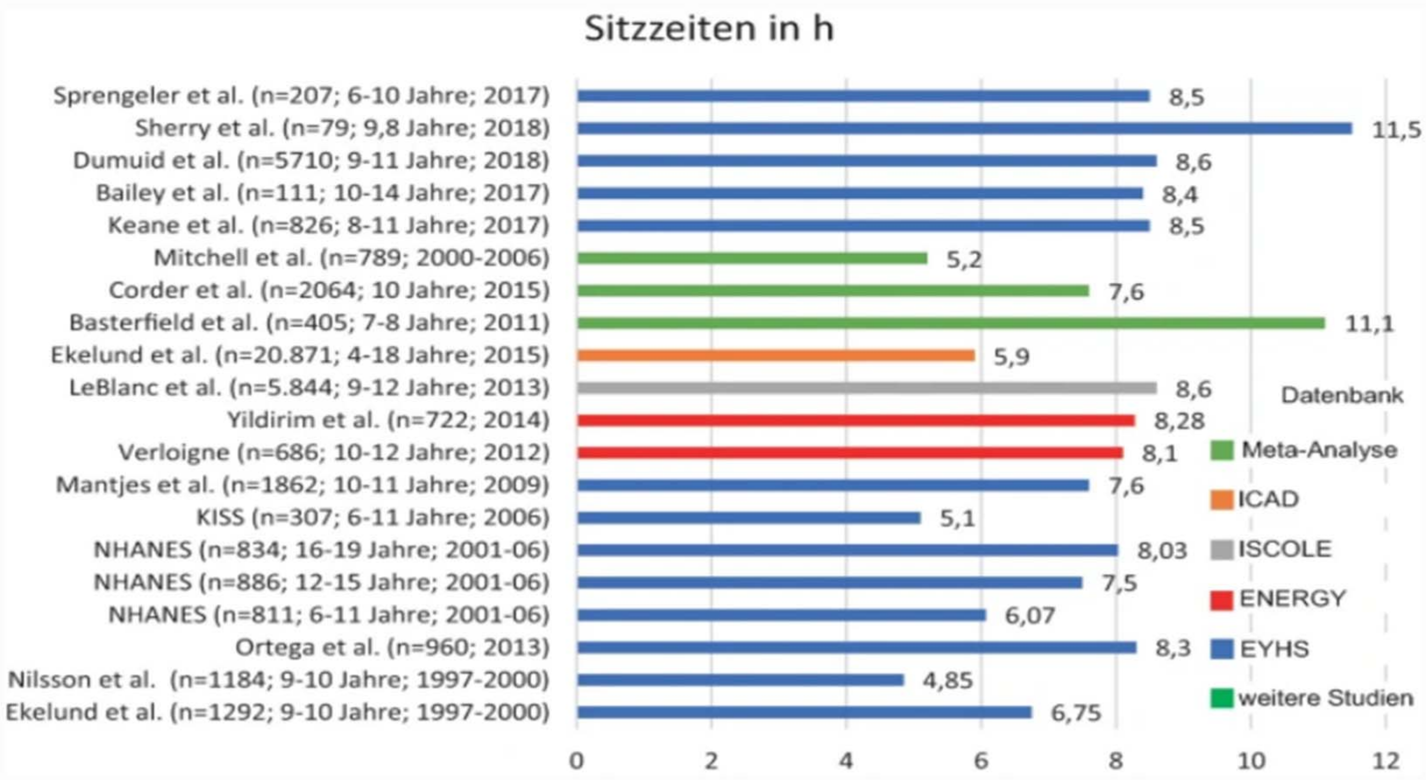
MacKelvie et al, *Bone* 2004;34:755

Daily Physical Activity and Bone Mass Development



Janz, KF et al., PEDIATRICS 2001

Abbildung 1.3

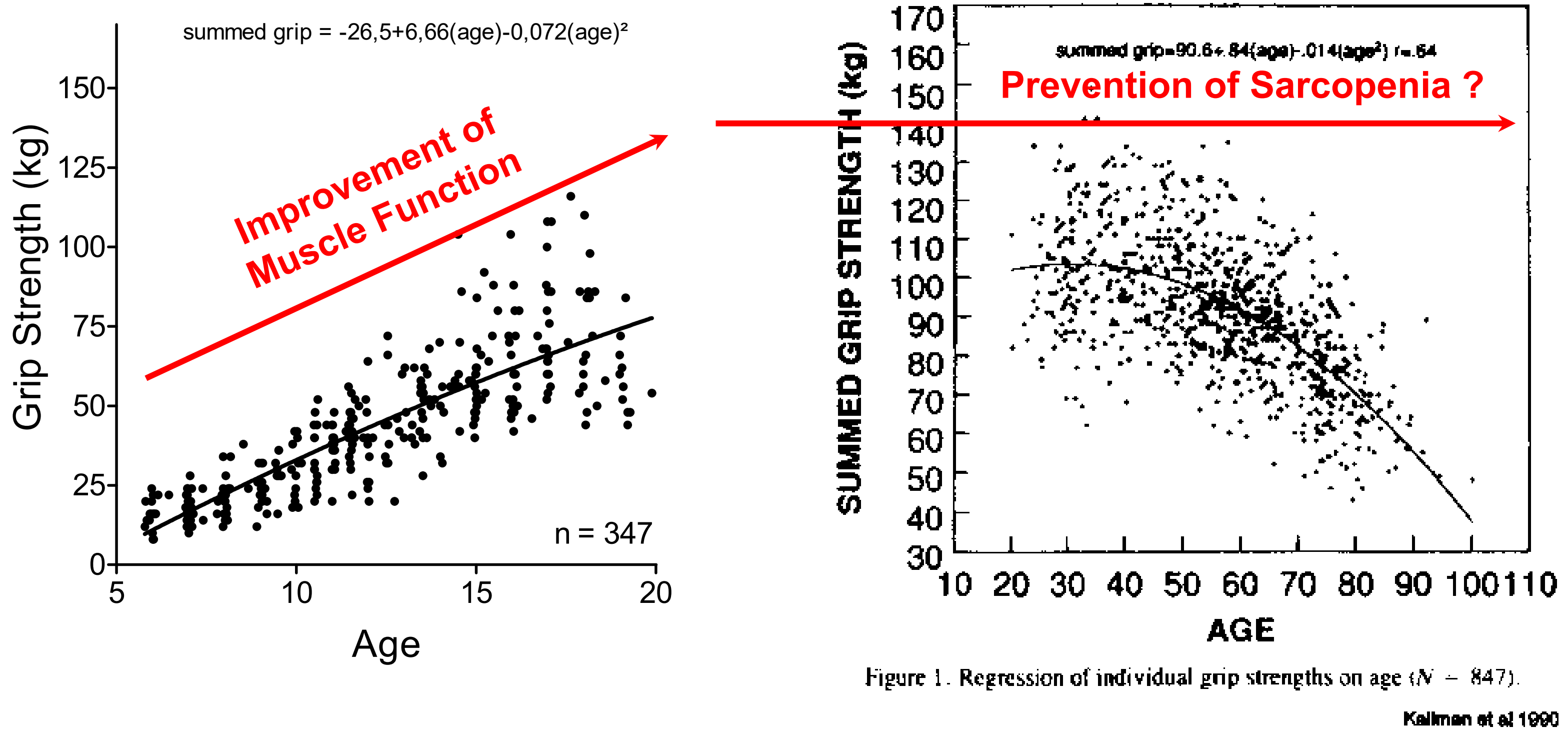


(eigener Entwurf)

Übersicht über repräsentative Studien zu Sitzzeiten von Kindern.

Wann sitzen wir nur noch ?

Zimmermann, R. (2022). Begriffe, Belege, Belastung. In: Bewegter Unterricht – reloaded!. Springer VS, Wiesbaden. https://doi.org/10.1007/978-3-658-37458-7_1


summed grip = -26,5+6,66(age)-0,072(age)²
Grip Strength (kg)
Age
n = 347
Improvement of Muscle Function
Prevention of Sarcopenia ?
SUMMED GRIP STRENGTH (kg)
AGE
Figure 1. Regression of individual grip strengths on age (N = 847).
Kallman et al 1990

Zitation: Schmidt, S.C.E, Burchartz, A., Kolb, S., Niessner, C., Oriwol, D., Hanssen-Doose, A., Worth, A. & Woll, A. (2021). Zur Situation der körperlich-sportlichen Aktivität von Kindern und Jugendlichen während der COVID-19 Pandemie in Deutschland: Die Motorik-Modul Studie (MoMo). *KIT Scientific Working Papers*, 165.

Bewegt in und durch das Leben ??

Ernährung dem Bewegungsausmaß angepasst ????

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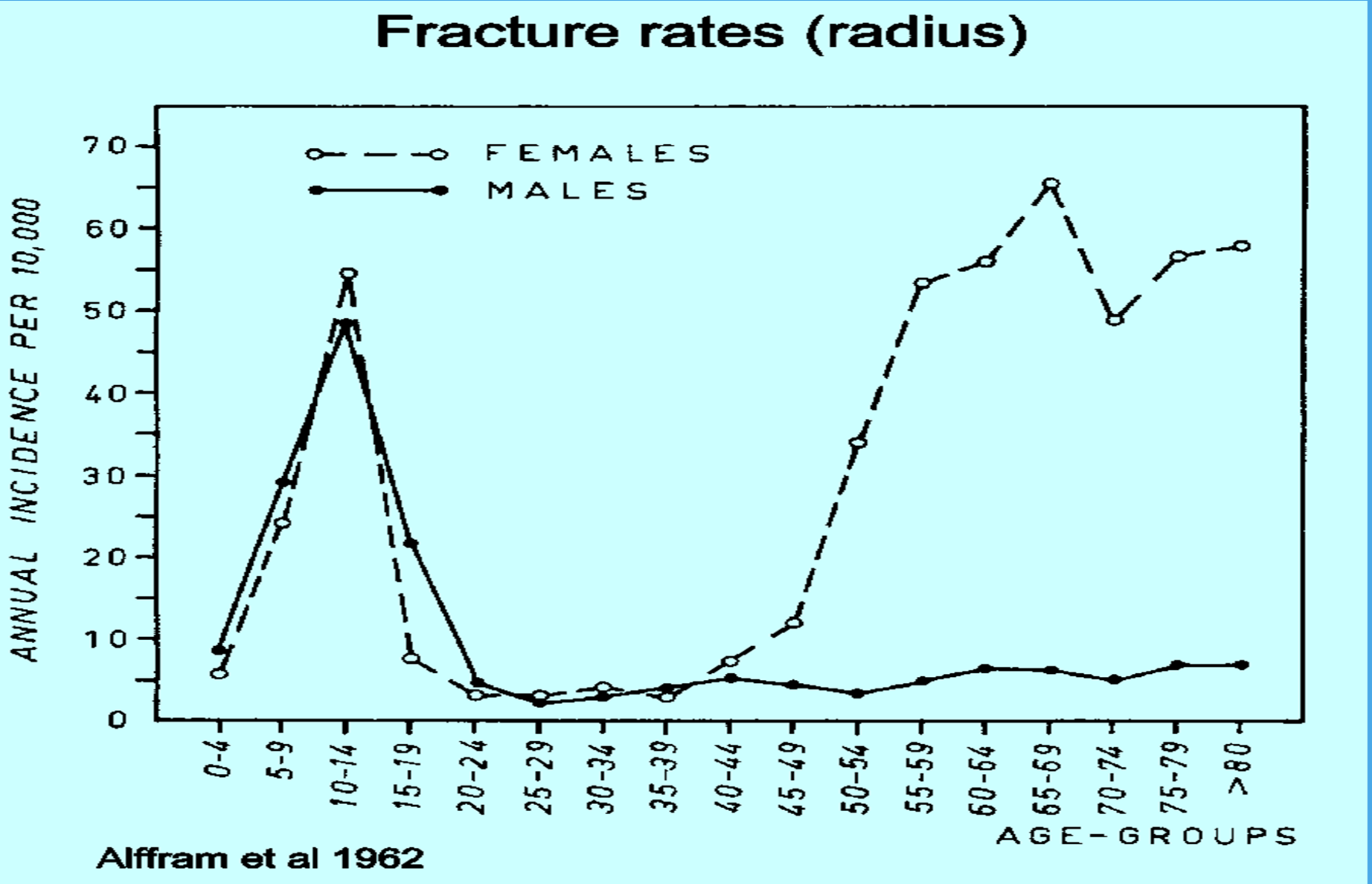
- 6. Frakturen

Altersabhängigkeit der Frakturen



Increase of Fracture Rates in Childhood

Table 1. Comparison of Age- and Sex-Specific Incidence Rates for Distal Forearm Fractures Among residents of Rochester, Minn, in 4 Time Periods Between 1969 and 2001

Age Group, y	1969-1971 No.	1969-1971 Incidence Rate (95% CI) per 100 000 Person-Years	1979-1981 No.	1979-1981 Incidence Rate (95% CI) per 100 000 Person-Years	1989-1991 No.	1989-1991 Incidence Rate (95% CI) per 100 000 Person-Years	1999-2001 No.	1999-2001 Incidence Rate (95% CI) per 100 000 Person-Years
Male Residents								
0-4	6	76.8 (28.2-167.2)	6	89.8 (33.0-195.6)	32	343.2 (234.7-484.5)	22	223.4 (140.0-338.2)
5-9	46	534.9 (391.6-713.5)	42	707.9 (510.2-956.9)	51	598.0 (445.3-786.3)	56	599.7 (453.0-778.7)
10-14	62	816.1 (625.7-1046.2)	58	898.9 (682.6-1162.1)	88	1266.9 (1016.1-1560.9)	124	1321.9 (1099.5-1576.2)
15-19	20	353.2 (215.7-545.4)	38	543.3 (384.5-745.8)	22	410.4 (257.2-621.3)	30	350.6 (236.6-500.5)
20-24	8	181.7 (78.4-357.9)	16	217.7 (124.4-353.5)	12	194.3 (100.4-339.3)	8	97.1 (41.9-191.4)
25-29	4	65.3 (17.8-167.3)	10	116.5 (55.9-214.2)	7	67.2 (27.0-138.5)	11	110.1 (55.0-197.0)
30-34	6	102.3 (37.5-222.6)	6	86.2 (31.6-187.5)	13	120.7 (64.3-206.5)	12	114.3 (59.1-199.7)
Subtotal*	152	309.4 (259.3-359.5)	176	385.7 (328.5-443.0)	225	433.9 (376.0-491.7)	263	409.4 (359.9-459.0)
Female Residents								
0-4	11	150.4 (75.1-269.1)	9	141.4 (64.6-268.3)	37	415.5 (292.5-572.7)	19	201.5 (121.3-314.7)
5-9	46	566.1 (414.4-755.1)	30	509.3 (343.6-727.1)	86	1097.5 (877.9-1355.4)	71	832.3 (650.1-1049.9)
10-14	36	490.9 (343.8-679.7)	39	634.7 (451.3-867.6)	38	579.1 (409.8-794.8)	73	799.5 (626.7-1005.2)
15-19	9	119.5 (54.6-226.9)	13	165.1 (87.9-282.4)	7	123.8 (49.8-255.1)	18	221.3 (131.1-349.7)
20-24	1	10.6 (0.3-59.2)	18	157.3 (93.2-248.6)	10	127.5 (61.1-234.5)	10	114.6 (55.0-210.8)
25-29	7	95.7 (38.5-197.2)	9	96.0 (43.9-182.3)	10	89.1 (42.7-163.9)	7	65.6 (26.4-135.2)
30-34	3	51.8 (10.7-151.4)	5	66.7 (21.6-155.6)	12	107.2 (55.4-187.3)	8	78.1 (33.7-153.9)
Subtotal*	113	214.6 (174.9-254.4)	123	255.4 (209.1-301.6)	200	363.6 (312.4-414.8)	206	334.3 (288.6-380.1)
Total†	265	263.3 (231.1-295.4)	299	322.3 (285.3-359.4)	425	399.8 (361.0-438.6)	469	372.9 (339.1-406.7)

Abbreviation: CI, confidence interval.
*Incidence per 100 000 person-years directly age-adjusted to the population structure of United States whites in 2000.
†Incidence per 100 000 person-years directly age- and sex-adjusted to the population structure of United States whites in 2000.

Khosla S et al., JAMA 2003

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- 6. Frakturen
- 7.Zusammenfassung

- Zusammenfassung
- 1. Das Muskelsystem mit seinen Kräften und das Skelettsystem mit seiner Festigkeit sind aufeinander abgestimmt.
- 2. Das Netzwerk der Osteozyten steuert das Zusammenspiel von
- Knochenaufbau und –abbau - kontinuierliche Adaption
- 3. Diese Mechanismen sprechen gegen lebenslänglich anhaltende Effekt.
- 4. Die Unterscheidung zwischen einer Knochenstruktur und –"härte"
- Störung gewährleistet eine problembezogene Therapie.
- 5. Es zeigt sich ein stets weiter zunehmender Bewegungsmangel.

- 6. Ernährung (Energie,Mineral,...)und Bewegung sollten aufeinander abgestimmt sein.
- 7. Frakturen im Kindes- und Jugendalter sind normal und zeigen eine gewisse Zunahme
- (Trampoline)
- 8. Der Entwicklung des Muskelsystem und der neuromuskulären Kompetenzen sollte mehr Aufmerksamkeit gewidmet werden.

Compr Physiol. Author manuscript; available in PMC 2014 Nov 23.

Published in final edited form as:

Compr Physiol. 2012 Apr; 2(2): 1143–1211.

doi: 10.1002/cphy.c110025

Lack of exercise is a major cause of chronic diseases

Frank W. Booth, Ph.D.,[1] Christian K. Roberts, Ph.D.,[2] and Matthew J. Laye, Ph.D.[3]

Quotations attributed to Hippocrates promote the primary prevention of disease by physical activity.

> *"If we could give every individual the right amount of nourishment and exercise, not too little and not too much, we would have found the safest way to health" (240).*
>
> *"If there is any deficiency in food and exercise the body will fall sick" (477).*
>
> *"Walking is man's best medicine" (240).*
>
> *"All parts of the body, if used in moderation and exercised in labors to which each is accustomed, become thereby healthy and well developed and age slowly; but if they are unused and left idle, they become liable to disease, defective in growth and age quickly" (278).*

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Lack of exercise is a major cause of chronic diseases

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5.2 Hippocrates (~450 BC)

Quotations attributed to Hippocrates promote the primary prevention of disease by physical activity.

> *"If we could give every individual the right amount of nourishment and exercise, not too little and not too much, we would have found the safest way to health" (240).*

> *"If there is any deficiency in food and exercise the body will fall sick" (477).*

> *"Walking is man's best medicine" (240).*

> *"All parts of the body, if used in moderation and exercised in labors to which each is accustomed, become thereby healthy and well developed and age slowly; but if they are unused and left idle, they become liable to disease, defective in growth and age quickly" (278).*

Danke für Ihre Aufmerksamkeit!

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