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Three-dimensional models of skeletal muscle under tension and methods to induce traumatic injury: systematic review search protocol

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# OPEN ACCESS



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Protocol status: Working
We use this protocol and it's
working

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## Abstract

#### Volumetric

muscle loss (VML) is defined as the significant loss of skeletal muscle as a result of traumatic injury or surgical intervention, resulting in functional and regenerative impairment. It is a considerable form of morbidity and is implicated in blast, penetrating or blunt trauma. Current research on VML is centred around models that are not specific to the injury patterns or environments usually encountered. In order to examine the effects of traumatic injury on skeletal muscle, more representative in vitro models are required to generate a deeper cellular picture prior to preclinical validation. Whilst in vivo models are invaluable, they are expensive and have a lower throughput platform for discovery research. The aim of this systematic review is to examine the types of in vitro muscle models that are applicable to understanding VML. We have therefore designed an inclusive search protocol to incorporate all relevant muscle models under tension and endeavour to subcategorise these depending on methods of inducing injury. "Skeletal muscle" was the major inclusion criterion, followed by "three dimensional" and "model". The Ovid interface was used to search MEDLINE, EMBASE and Web of Science Core Collection databases to yield 4,895 eligible articles after de-duplication. As of 30/05/2024 articles are in the process of being blindly screened by two independent reviewers. Major inclusion criteria are three dimensional in vitro models under tension. A sub analysis will subsequently be performed to examine how injury is induced in such muscle models.



### Methods

- This systematic review was reported in compliance with the PRISMA 2020 checklist. The protocol was developed prospectively in collaboration with a research librarian (NT) at the Nuffield Department of Rheumatology and Musculoskeletal Sciences (NDORMS).
- All databases were searched from inception until 13/03/2024. The Ovid interface was used to search MEDLINE (1946-present), EMBASE (1974-present) and Web of Science Core Collection (1900-present) databases. No date or language limits were applied. Synonyms were produced in line with elements of the research question. "Skeletal muscle" was the major inclusion criterion, followed by "three dimensional" and "model". Synonyms for skeletal muscle included "myotube", "slow-twitch muscle fibres" and "fast-twitch muscle fibres". Synonyms for "three-dimensional" included "3D", "organoid" and "lab on a chip". Synonyms for "model" included "scaffold", "architecture" and "platform". Full search strategies can be found in the appendix.

#### Inclusion criteria

In vitro studies that utilised any skeletal muscle cell lines (primary or immortalised, single or multicellular) of any species cultured with an anchor system were eligible for inclusion. Models that used organic hydrogel compounds native to the human body (fibrin or collagen) were included. Where studies reported minor experimental modifications of previously reported models (with detailed methods), the most comprehensive study or studies were included.

#### Exclusion criteria

Models that did not impose axial strain or loading, self-assembly models (spheroids etc) or tissue explant models (including slice culture) were excluded. In vitro models that cultured cells on patterned surfaces (to include orientation) were also excluded, even if they used 3D systems. In vitro monolayer systems were excluded. Ex vivo perfusion systems were also excluded. Models that synthesised hydrogels using materials that were incapable of biodegradation (breakdown of organic matter into constituent elements) within humans (or human tissue) were excluded. Studies without detailed methods, opinion pieces, reviews, letters, conference abstracts, in vivo work and book chapters were excluded.

## **Appendix**

5 EMBASE search:

Total Records downloaded (enter this number here to	1970	
update		



SearchReport tab):			
Search Strategy			
Embase 1974 to present			
1	skeletal myoblast/	596	
2	(skeletal adj2 myoblast*).tw,kf.	2170	
3	skeletal muscle cell line/	83	
4	(cell* adj2 (stem or primary or satellite)).tw,kf.	624478	
5	(myogenic or skeletal muscle).tw,kf.	172977	
6	4 and 5	11204	
7	skeletal muscle/	144693	
8	slow muscle fiber/	2149	
9	fast muscle fiber/	2212	
10	10	skeletal.tw,kf.	299053
10			
11	(muscle* adj2 fiber*).tw,kf.	35259	



		Г
12	10 and 11	13999
13	(fast-twitch or intermediate or white or type II).tw,kf.	1117798
14	(red or slow-twitch or type I).tw,kf.	630013
15	13 or 14	1657758
16	11 and 15	6707
17	myotube*.tw,kf.	15390
18	(skeletal adj2 myocyte*).tw,kf.	751
19	(myogenic or skeletal muscle).tw,kf.	172977
20	(cell* adj2 c2c12).tw,kf.	6130
21	19 and 20	3398
22	1 or 2 or 3 or 6 or 7 or 8 or 9 or 12 or 16 or 17 or 18 or 21	171236
23	3d.tw,kf.	324905
24	three d.tw,kf.	638
25	3 dimension*.tw,kf.	38685
26	organoid/	13217
27	organoid*.tw,kf.	23541



28	exp lab on a chip/	11240
29	lab on a chip.tw,kf.	3765
30	organ on a chip.tw,kf.	1453
31	exp bioengineering/	235895
32	bioengineer*.tw,kf.	15596
33	biological engineer*.tw,kf.	1427
34	tissue engineer*.tw,kf.	80668
35	23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34	628442
36	22 and 35	3934
37	model*.tw,kf.	5000672
38	scaffold*.tw,kf.	158968
39	architecture*.tw,kf.	197564
40	platform*.tw,kf.	357571
41	(system or systems).tw,kf.	4417710
42	37 or 38 or 39 or 40 or 41	8919326
43	36 and 42	2505
44	conference*.pt.	5859448



<u> </u>			
45	43 not 44	1970	

#### 6 MEDLINE search:

Total Records downloaded (enter this number here to update SearchReport tab):	2650	
Search Strategy		
Medline (Ovid MEDLINE‱ Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE‱ Daily and Ovid MEDLINE‱) 1946 to present		
1	exp Myoblasts, Skeletal/	4090
2	(skeletal adj2 myoblast*).tw,kf.	1795
3	(cell* adj2 (stem or primary or satellite)).tw,kf.	422521
4	(myogenic or skeletal muscle).tw,kf.	139662
5	3 and 4	8576
6	Muscle, Skeletal/	166516
7	Muscle Fibers, Skeletal/	17604
8	Muscle Fibers, Slow-	2488



Ī	Twitch/		
9	Muscle Fibers, Fast- Twitch/	3131	
10	skeletal.tw,kf.	237495	
11	11	(muscle* adj2 fiber*).tw,kf.	29880
11			
12	10 and 11	11474	
13	(fast-twitch or intermediate or white or type II).tw,kf.	844075	
14	(red or slow-twitch or type I).tw,kf.	493609	
15	13 or 14	1266664	
16	11 and 15	5555	
17	myotube*.tw,kf.	12495	
18	(skeletal adj2 myocyte*).tw,kf.	600	
19	(myogenic or skeletal muscle).tw,kf.	139662	
20	(cell* adj2 c2c12).tw,kf.	4658	
21	19 and 20	2556	



22	1 or 2 or 5 or 6 or 7 or 8 or 9 or 12 or 16 or 17 or 18 or 21	193945	
23	3d.tw,kf.	249537	
24	three d.tw,kf.	468	
25	3 dimension*.tw,kf.	29970	
26	Organoids/	13773	
27	27	organoid*.tw,kf.	15510
27			
28	Lab-On-A-Chip Devices/	7533	
29	lab on a chip.tw,kf.	3690	
30	organ on a chip.tw,kf.	1382	
31	exp Bioengineering/	62819	
32	bioengineer*.tw,kf.	12040	
33	biological engineer*.tw,kf.	432	
34	Tissue Engineering/	45681	
35	tissue engineer*.tw,kf.	64407	



36	23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35	387881
37	22 and 36	3428
38	model*.tw,kf.	3967863
39	scaffold*.tw,kf.	135360
40	methods.fs.	4360174
41	architecture*.tw,kf.	172933
42	platform*.tw,kf.	271052
43	(system or systems).tw,kf.	3641694
44	38 or 39 or 40 or 41 or 42 or 43	10499757
45	37 and 44	2650

#### 7 Web of science search strategy:

Search

Strategy

# Search Query Database Results

1 "myotube OR (skeletal NEAR/2

myoblast\*) OR ""skeletal muscle"" OR ""fast

twitch muscle fibre\*"" OR ""slow twitch muscle

fibre\*"" OR (skeletal NEAR/2 myocyte\*) (Topic) AND 3d OR ""three

dimension\*"" OR ""three d"" OR organoid\* OR

""lab on a chip"" OR ""organ on a

chip"" OR bioengineer\* OR ""tissue engineer\*"" OR

""biological engineer\*""

(Topic) AND model\* OR scaffold\* OR architecture\* OR platform\* OR system

OR systems (Topic)



Web of

Science Core Collection 2811