KEMENTERIAN PENDIDIKAN DAN KEBUDAYAAN
UNIVERSITAS AIRLANGGA
Kampus C Mulyorejo Surabaya 60115 Telp. (031) 5914042, 5914043, Fax (031) 5981841
Laman : http://www.unair.ac.id; e-mail : rektor@unair.ac.id

SALINAN

KEPUTUSAN
REKTOR UNIVERSITAS AIRLANGGA
NOMOR 212/UN3/2021

TENTANG

PELAKSANAAN PENELITIAN INTERNAL
SKEMA HIBAH RISET MANDAT TOP TIER, HIBAH RISET KOLABORASI MITRA LUAR NEGERI, HIBAH MANDAT *ARTICLE REVIEW*, PENELITIAN UNGGULAN FAKULTAS DAN PENELITIAN DOSEN PEMULA TAHUN 2021 DILINGKUNGAN UNIVERSITAS AIRLANGGA

REKTOR UNIVERSITAS AIRLANGGA,

Menimbang : a. bahwa sesuai hasil seleksi proposal penelitian skema hibah riset mandat top tier, hibah riset mandat kolaborasi mitra luar negeri, hibah mandat *article review*, penelitian unggulan fakultas dan penelitian dosen Pemula Universitas Airlangga Tahun 2021 sebagai salah satu wujud dari pelaksanaan tridharma perguruan tinggi, maka perlu menetapkan para peneliti dan judul penelitian dimaksud;

b. bahwa berdasarkan pertimbangan sebagaimaan dimaksud pada huruf a, perlu menetapkan Keputusan Rektor tentang Pelaksanaan Penelitian Internal Skema Hibah Riset Mandat Top Tier, Hibah Riset Kolaborasi Mitra Luar Negeri, Hibah Mandat *Article Review*, Penelitian Unggulan Fakultas Dan Penelitian Dosen Pemula Tahun 2021 Dilingkungan Universitas Airlangga;

Mengingat : 1. Undang–Undang Nomor 20 Tahun 2003 tentang Sistem Pendidikan Nasional (Lembaran Negara Republik Indonesia Tahun 2003 Nomor 78, Tambahan Lembaran Negara Nomor 4301);

2. Undang–Undang Nomor 12 Tahun 2012 tentang Pendidikan Tinggi (Lembaran Negara Republik Indonesia Tahun 2012 Nomor 158, Tambahan Lembaran Negara Tahun 2012 Nomor 5336);

3. Peraturan Pemerintah Nomor 57 Tahun 1954 tentang Pendirian Universitas Airlangga di Surabaya sebagaimana telah diubah dengan Peraturan Pemerintah Nomor 3 Tahun 1955 tentang Pengubahan Peraturan Pemerintah Nomor 57 Tahun 1954 (Lembaran Negara Republik Indonesia Tahun 1954 Nomor 99 Tambahan Lembaran Negara Nomor 695 juncto Lembaran Negara Republik Indonesia Tahun 1955 Nomor 4 Tambahan Lembaran Negara Nomor 748);

4. Peraturan Pemerintah Nomor 37 Tahun 2009 tentang Dosen (Lembaran Negara Republik Indonesia Tahun 2009 Nomor 76, Tambahan Lembaran Negara Republik Indonesia Nomor 5007);

5. Peraturan Pemerintah Nomor 4 Tahun 2014 tentang Penyelenggaraan Pendidikan Tinggi dan Pengelolaan Perguruan Tinggi (Lembaran Negara Republik Indonesia Tahun 2014 Nomor 16, Tambahan Lembaran Negara Nomor 5500);

6. Peraturan Pemerintah Nomor 30 Tahun 2014 tentang Statuta Universitas Airlangga (Lembaran Negara Republik Indonesia Tahun 2014 Nomor 100, Tambahan Lembaran Negara Nomor 5535);
7. Peraturan Pemerintah Nomor 8 Tahun 2020 tentang Perubahan Atas Peraturan Pemeerintah Nomor 26 Tahun 2015 tentang Bentuk dan Mekanisme Pendanaan Perguruan Tinggi Negeri Badan Hukum (Lembaran Negara Republik Indonesia Tahun 2020 Nomor 28, Tambahan Lembaran Negara Republik Indonesia Nomor 6461);
8. Peraturan Presiden Nomor 72 Tahun 2019 tentang Kementerian Pendidikan dan Kebudayaan (Lembaran Negara Republik Indonesia Tahun 2019 Nomor 207);
9. Keputusan Majelis Wali Amanat Universitas Airlangga Nomor 3/UN3.MWA/K/2020 tentang Pengangkatan Rektor Universitas Airlangga Periode 2020-2025;
10. Peraturan Rektor Universitas Airlangga Nomor 39 Tahun 2017 tentang Perubahan Atas Peraturan Rektor Nomor 42 Tahun 2016 tentang Organisasi dan Tata Kerja Universitas Airlangga;
11. Peraturan Rektor Universitas Airlangga Nomor 11 Tahun 2020 tentang Pedoman Pendidikan Universitas Airlangga;
12. Keputusan Rektor Universitas Airlangga Nomor 865/UN3/2020 tentang Penggabungan Lembaga Pengabdian dan Pengembangan Masyarakat dan Lembaga Penelitian dan Inovasi Menjadi Lembaga Penelitian dan Pengabdian Masyarakat;
13. Keputusan Rektor Universitas Airlangga Nomor 913/UN3/2020 tentang Pemberhentian dan Pengangkatan Ketua Lembaga Universitas Airlangga;

Memperhatikan : Surat Ketua Lembaga Penelitian dan Pengabdian Kepada Masyarakat Universitas Airlangga Nomor 707/UN3.15/PT/2021, tanggal 13 April 2021, perihal Permohonan Keputusan Rektor tentang Pelaksanaan Penelitian Internal Universitas Airlangga Tahun 2021.

MEMUTUSKAN :

MENETAPKAN : **KEPUTUSAN REKTOR TENTANG PELAKSANAAN PENELITIAN INTERNAL SKEMA HIBAH RISET MANDAT TOP TIER, HIBAH RISET KOLABORASI MITRA LUAR NEGERI, HIBAH MANDAT *ARTICLE REVIEW*, PENELITIAN UNGGULAN FAKULTAS DAN PENELITIAN DOSEN PEMULA TAHUN 2021 DILINGKUNGAN UNIVERSITAS AIRLANGGA.**

KESATU : Menetapkan hasil seleksi proposal penelitian skema hibah riset mandat top tier, hibah riset mandat kolaborasi mitra luar negeri, hibah mandat *article review*, penelitian unggulan fakultas dan penelitian dosen pemula Universitas Airlangga Tahun 2021.

KEDUA : Penerima penelitian sebagaimana dimaksud pada diktum KESATU adalah sebagai berikut :

1. 10 (sepuluh) judul Penelitian Hibah Riset Mandat Top Tier;
2. 53 (lima puluh tiga) judul Penelitian Hibah Riset Mandat Kolaborasi Mitra Luar Negeri;
3. 6 (enam) judul Penelitian Hibah Mandat *Article Review*;
4. 259 (dua ratus lima puluh sembilan) judul Penelitian Unggulan Fakultas; dan
5. 70 (tujuh puluh) judul Penelitian Dosen Pemula,

dengan susunan nama tim peneliti sebagaimana tercantum dalam lampiran I, II, III, IV, dan V yang merupakan bagian tidak terpisahkan dari Keputusan Rektor ini.

KETIGA : Biaya untuk pelaksanaan penelitian sebagaimana dimaksud pada diktum KEDUA adalah:

1. Penelitian Hibah Riset Mandat Top Tier sebesar Rp. 2.245.973.000,- (dua milyar dua ratus empat puluh lima juta sembilan ratus tujuh puluh tiga ribu rupiah) dibebabankan pada dana RKAT Lembaga Penelitian dan Pengabdian Kepada Masyarakat;
2. Penelitian Hibah Riset Mandat Kolaborasi Mitra Luar Negeri sebesar Rp. 5.273.242.000,- (lima milyar dua ratus tujuh puluh tiga juta dua ratus empat puluh dua ribu rupiah) dibebabankan pada dana RKAT Lembaga Penelitian dan Pengabdian Kepada Masyarakat;
3. Penelitian Hibah Mandat *Article Review* sebesar Rp. 292.000.000,- (dua ratus sembilan puluh dua juta rupiah) dibebabankan pada dana RKAT Lembaga Penelitian dan Pengabdian Kepada Masyarakat;
4. Penelitian Unggulan Fakultas sebesar Rp. 9.211.662.710,- (sembilan milyar dua ratus sebelas juta enam ratus enam puluh dua ribu tujuh ratus sepuluh rupiah) dibebankan pada RKAT masing-masing Fakultas; dan
5. Penelitian Dosen Pemula sebesar Rp. 1.467.387.900,- (satu milyar empat ratus enam puluh tujuh juta tiga ratus delapan puluh tujuh ribu sembilan ratus rupiah) dibebankan pada RKAT masing-masing Fakultas.

KEEMPAT : Dalam melaksanakan tugasnya, penerima dana penelitian sebagaimana dimaksud pada diktum KEDUA, harus bekerja secara jujur dan transparan dengan berpedoman pada ketentuan peraturan perundang-undangan yang berlaku, serta bertanggungjawab kepada Rektor melalui Dekan pada Fakultas masing-masing.

KELIMA : Jangka waktu pelaksanaan penelitian sebagaimana dimaksud pada diktum KESATU mulai tanggal 1 Maret sampai dengan 31 Desember 2021.

KEENAM : Keputusan Rektor ini mulai berlaku pada tanggal ditetapkan dan memiliki daya laku surut sejak 1 Maret 2021.

Salinan disampaikan Yth:
1. Pimpinan Unit Kerja di Lingkungan UNAIR;
2. Yang bersangkutan.

Ditetapkan di Surabaya
pada tanggal 22 April 2021

REKTOR,

TTD

MOHAMMAD NASIH
NIP.196508061992031002

Salinan sesuai dengan aslinya
Sekretaris Universitas,

KOKO SRIMULYO
NIP 196602281990021001

LAMPIRAN II KEPUTUSAN REKTOR UNIVERSITAS AIRLANGGA
NOMOR : 212/UN3/2021, TANGGAL 22 APRIL 2021
TENTANG : PELAKSANAAN PENELITIAN INTERNAL SKEMA HIBAH RISET MANDAT TOP TIER, HIBAH RISET KOLABORASI MITRA LUAR NEGERI, HIBAH MANDAT ARTICLE REVIEW, PENELITIAN UNGGULAN FAKULTAS DAN PENELITIAN DOSEN PEMULA TAHUN 2021 DI LINGKUNGAN UNIVERSITAS AIRLANGGA

DAFTAR PROPOSAL PENELITIAN HIBAH RISET MANDAT KOLABORASI MITRA LUAR NEGERI YANG LOLOS DIDANAI TAHUN 2021

No	Tim Penelitian	NIP	Nama Mitra	Nama Mahasiswa	NIM	Skema Penelitian	Fakultas	Riset Grup	Judul Penelitian	DANA
1	Prof. Soedjajadi, dr., M.S., Ph.D. Dr. Lilis Sulistyorini, Ir., M.Kes Muhammad Farid Dimjati Lusno, dr., M.KL	195203151979031008 196603111991032002 197204242008121002	Saliza Binti Mohd Elias, Ph.D	YUDHIAKUARI SINCIHU ELLYZA SETYA MARYIANTARI	101917087303 101817087302	Hibah Riset Mandat Kolaborasi Mitra Luar Negeri	Kesehatan Masyarakat	Biomarker Of Exprosure To Hazardous Material	MEKANISME PENURUNAN FUNGSI KOGNITIF MELALUI KEMATIAN SEL NEURON OTAK RATTUS NORVEGICUS STRAIN WISTAR AKIBAT PEMBERIAN MAKANAN MENGANDUNG MIKROPLASTIK SEKUNDER PERORAL	Rp 99.810.000
2	Trias Mahmudiono, S.KM., M.P.H., Ph.D. Dr. Mahmudah, Ir., M.Kes. Qonita Rachmah, S.Gz., M.Sc.	198103242003121001 196901101993032002 199102152018083201	Dr. Loh Su Peng	EURIKA ZEBADIA RELAWANTRIA HARLIANTI	101711233055 101711233050	Hibah Riset Mandat Kolaborasi Mitra Luar Negeri	Kesehatan Masyarakat	Center For Health And Nutrition Education, Conseling, And Empowerment (ChENECE)	Pendidikan Gizi 4.0 untuk Mencegah Gizi Lebih dan Obesitas Melalui Kampanye Media Sosial	Rp 100.000.000
3	Laura Navika Yamani, S.Si., M.Si., Ph.D. Muhammad Atoillah Isfandiari, dr., M.Kes Dr. Santi Martini, dr., M.Kes	198601082018032001 197603252003121002 196609271997022001	Prof. Chung Yi Li, Ph.D	ALIFIA SALMA PANGESTIKA NUR SAHILA	101811133126 101811133159	Hibah Riset Mandat Kolaborasi Mitra Luar Negeri	Kesehatan Masyarakat	Tropical Diseases, Infectious Diseases, and Herb	ANALISIS SEROSURVEI VAKSIN COVID-19 DI SURABAYA, INDONESIA	Rp 100.000.000
4	Prof. Dr. Moh. Nasih, S.E., M.T., Ak., CM.A., CA. Iman Harymawan, S.E., M.BA., Ph.D.	196508061992031002 198404202008121005	Dr. John Nowland	DAMARA ARDELIA KUSUMA WARDANI EKA SARI AYUNINGTYAS	042014253007 041914253026	Hibah Riset Mandat Kolaborasi Mitra Luar Negeri	Ekonomi dan Bisnis	Center for Political Economy and Business Research	CORPORATE GOVERNANCE AND AUDIT FEE	Rp 100.000.000
5	Prof. Dr. Ir. Agoes Soegianto, DEA. Trisnadi Widyaleksono C.P, Drs., M.Si.	196208031987101001 196312151989031002	Carolyn Melissa Payus	fauzan muhammad eddin Andhika Bima Pratama	081711133043 081711133047	Hibah Riset Mandat Kolaborasi Mitra Luar Negeri	Sains dan Teknologi	Grup Riset Teknologi dan Inovasi Lingkungan	PENGARUH KEGIATAN ANTROPOGENIK TERHADAP PRODUKTIVITAS TAMBAK UDANG DAN KUALITAS HASIL LAUT	Rp 100.000.000
6	Dr. Mulyadi Tanjung, Drs., M.S. Prof. Tjitjik Srie Tjahjandarie, Dra., Ph.D.	196504221991021001 196502061988102001	Prof. Norizan Ahmat, Ph.D	Diah Ayu Rachmawati SHOLA MARDHIYYAH	081711533001 081711533058	Hibah Riset Mandat Kolaborasi Mitra Luar Negeri	Sains dan Teknologi	Kimia Organik Bahan Alam (KOBA)	EKSPLORASI SENYAWA BARU TERPENIL-STILBEN DARI Mearanga gigantea SEBAGAI KANDIDAT OBAT KANKER	Rp 100.000.000
7	Dr. Mas Rahmah, S.H., M.H., LL.M. Nurul Barizah, S.H., LL.M., Ph.D	197109121998022001 197102221995122002	Prof. Sam Blay Prof. Christoph Antons	Arsasti Satya Pradyta Adhisty Radhita Vasya	031711133040 032011133120	Hibah Riset Mandat Kolaborasi Mitra Luar Negeri	Hukum	Grup Riset Hak Kekayaan Intelektual, Bio Teknologi dan Industri Kreatif	PENGADAAN VAKSIN MURAH DAN OBAT ESENSIAL UNTUK COVID-19 MELALUI PELAKSANAAN PATEN OLEH PEMERINTAH (GOVERNMENT USE) UNTUK MENJAMIN KETERSEDIAAN DAN KETERJANGKAUAN SERTA KEMANDIRIAN VAKSIN NASIONAL DEMI KESEHATAN MASYARAKAT	Rp 100.000.000
8	Dr. Lutfi Agus Salim, SKM., M.Si. Dr. Hj. Rr. Soenarnatalina Melaniani, Ir., M.Kes. Nurul Fitriyah, S.KM., M.P.H.	197008201997021001 196012251990032001 197511212005012002	Associate Professor Dr. Hanita Bt Daud Dr. Mahmod Bin Othman	YULY SULISTYORINI MUTHMAINNAH AILSA LAILY SAFIRA	102017087316 102017087319 012011133266	Hibah Riset Mandat Kolaborasi Mitra Luar Negeri	Kesehatan Masyarakat	Population And Sustainable Development	Analisis Pengaruh Pengendalian Penduduk Terhadap Pembangunan Sosial Ekonomi (Studi komparasi antara Indonesia dan Malaysia)	Rp 99.910.000
9	Prof. Muchammad Yunus, drh., M.Kes., Ph.D. Dr. Endang Suprihati, drh., M.S. Agus Sunarso, drh., M.Sc.	196612291993031001 195810211983112001 196708061994031001	Prof. Hiroshi Sato, DVM., Ph.D	ABHIRAMA ZABDIKA PRASETYA Riska Ayu Wilujeng	061711133176 061611133091	Hibah Riset Mandat Kolaborasi Mitra Luar Negeri	Kedokteran Hewan	PARASIT- HEWAN	Pengembangan Diagnosa dan Assessment Myxosporidiosis Asymptomatic melalui Microplastic Identification dalam Upaya Pencegahan Penularan dan Penyebaran pada Ikan Budidaya	Rp 100.000.000

No	Tim Penelitian	NIP	Nama Mitra	Nama Mahasiswa	NIM	Skema Penelitian	Fakultas	Riset Grup	Judul Penelitian	DANA
20	Dr. Eko Prasetyo Kuncoro, S.T., DEA. Dr. Handoko Darmokoesoemo, Drs., M.Sc. Thin Soedarti, dra., CESA	197508302008121001 196211021988101001 196709201992032001	Dr. Erio Gubal	RIFQA DYAH PUSPITA AMIRATUDZ DZAKIYAH AL-ULA PRIMALDO MARMORA HAQ	081811133028 081811133049 081811133037	Hibah Riset Mandat Kolaborasi Mitra Luar Negeri	Sains dan Teknologi	Grup Riset Teknologi dan Inovasi Lingkungan	Pemanfaatan limbah cangkang kerang hijau (Perna viridis) dan kerang bulu (Anadara antiquata) sebagai adsorbent murah untuk penyisihan tembaga, nikel dan seng: waste valorisation untuk pengendalian pencemaran air	Rp 100.000.000
21	Rico Ramadhan, S.Si., M.P., Ph.D. Kautsar Ul Haq, S.Si., M.Si. Dr. Hery Suwito, Drs., M.Si.	198506182018083101 199310132018083101 196303081987011001	Prof Preecha Phuwapraisirisan, Ph.D	HANDIKA FERDIANSYAH IRMAYANTI TRI KURNIA	081711533050 081711533030	Hibah Riset Mandat Kolaborasi Mitra Luar Negeri	Sains dan Teknologi	Exploration and synthesis of bioactive compounds BIOME	Exploration of bioactive compounds from East Kalimantan ethnomedicinal plants as antidiabetic agents concomitantly inhibiting alpha-glucosidase and free radicals	Rp 100.000.000
22	Kiki Adi Kurnia, S.Si., M.Sc., Ph.D. Dr. Laksmi Sulmartiwi, S.Pi., M.P. Eka Saputra, S.Pi., M.Si.	198112242019056101 197203021997022001 198610252015041002	Professor Joao A.P. Coutinho	REVANDA RIZKY PUTRAISYA ARFIAN DEWANANDA	141711233055 141711233058	Hibah Riset Mandat Kolaborasi Mitra Luar Negeri	Perikanan dan Kelautan	Post-harvest, Fish Processing and Fisheries Bio-products	Peningkatan aktivitas antioksidan dan analisa komponen bioaktif kerang pisau (Solen sp.) dengan menggunakan pelarut hijau berbantu gelombang mikro	Rp 100.000.000
23	Muhamad Amin, S.Pi., M.Sc., Ph.D. Syifania Hanifah Samara, S.Pi., M.Sc.	198110102019083101 198804142018032001	Rara Diantari, S.Pi., M.Sc Olumide Odeyemi	M. GIANO FADHILAH ZULFA AROFATUL JANNAH	141811133072 141711133065	Hibah Riset Mandat Kolaborasi Mitra Luar Negeri	Perikanan dan Kelautan	Fish Nutrition	Identifikasi jenis pakan larva lobster pasir (Panulirus homarus) sebagai dasar pengembangan teknologi produksi benih lobster secara buatan	Rp 100.000.000
24	Dr. Nanik Siti Aminah, M.Si. Dr. Alfinda Novi Kristanti, dra., DEA.	196705141991022001 196711151991022001	Dr. Khun Nay Win Tun Assoc. Prof. Dr. Yoshiaki Takaya	MILA ROSYDA ANDIKA PRAMUDYA WARDANA	082014253001 082017027306	Hibah Riset Mandat Kolaborasi Mitra Luar Negeri	Sains dan Teknologi	Bioteknologi Tanaman Obat	Eksplorasi Senyawa Bioaktif dari Tumbuhan Tropis Terseleksi	Rp 100.000.000
25	Sulikah Asmorowati, S.Sos., M. Dev.S.T., Ph.D. Prof. Dr. Jusuf Irianto, Drs., M.Com	197505161999032003 196505061993031003	Dr. Violeta Schubert	Siti Khodijah Ananda Ayu SASKIA RIZQINA MAULIDA Pryanka Pendu AYU PUSPITA NINGRUM	071711133092 071711133047 071811133018 071711133043	Hibah Riset Mandat Kolaborasi Mitra Luar Negeri	Ilmu Sosial dan Ilmu Politik	Centre for public policy, Governance and Development (CPPGD)	Feminisation of transnational migration, stateless children and pro-children development: An intersectionality-based policy analysis of Kabupaten/Kota Layak Anak (KLA) in Tulungagung and Ponorogo	Rp 100.000.000
26	Dr. Ririn Tri Ratnasari, S.E., M.Si. Prof. Dr. Raditya Sukmana, S.E., M.A. Dr. Achsania Hendratmi, S.E., M.Si.	197511262005012002 197604132002121003 197512302010122001	Associate Prof. TS. Dr. Aidi Ahmi Associate Professor Mohamed Battour, MSc., Ph.D	Zhazha Quamilla AHMAD KHABIB DWI ANGGARA	041611433011 041711433177	Hibah Riset Mandat Kolaborasi Mitra Luar Negeri	Ekonomi dan Bisnis	Center for Halal Industry Digitalization (CHID)	Designing a Halal Ecosystem Development Model to Support Indonesia's Economic Growth Post-Covid-19 Pandemic : Comparative Study of Indonesia, Malaysia and the United Arab Emirates	Rp 100.000.000
27	Dr. Woro Hastuti Satyantini. Ir., M.Si. Kiki Adi Kurnia, S.Si., M.Sc., Ph.D. Patmawati, S.Pi.,M.Si.	196109071989032001 198112242019056101 198803212019032013	Sonia Ventura	ALVIRA FEBRIANTI PRATIWI Akmal Yusuf Haryadi	142015353009 141711233068	Hibah Riset Mandat Kolaborasi Mitra Luar Negeri	Perikanan dan Kelautan	Post-harvest, Fish Processing and Fisheries Bio-products	POTENSI ANTI BAKTERI DAN ANTIOKSIDAN BAHAN BIOAKTIF RUMPUT LAUT HIJAU (Caulerpa sp.) SEBAGAI BAHAN IMUNOSTIMULAN	Rp 100.000.000
28	Prof. Dr. Retna Apsari, M.Si. Samian, S.Si., M.Si. Prof. Dr. Moh. Yasin, Drs., M.Si.	196806261993032003 196706211998021001 196703121991021001	Sulaiman Wadi Harus	ARSITA DEVIA RENSY PUTRI PRAMESYANTI	081811333002 081811333019	Hibah Riset Mandat Kolaborasi Mitra Luar Negeri	Sains dan Teknologi	Photonics Research Group	Ultrafast Ytterbium-doped Fiber Laser Mode-locked by a MAX phase based Saturable Absorber	Rp 100.000.000
29	Devi Rianti, drg., M.Kes. Tansza Permata Setiana Putri, drg., Ph.D.	196309071990022001 198909282019086201	Dr. Ir. Adriyansyah Syahrom, M Eng.	Geo Fanny Rania Vivian Nathania	021711133130 021711133129	Hibah Riset Mandat Kolaborasi Mitra Luar Negeri	Kedokteran Gigi	Tissue Engineering & Regenerative Medicine	POTENSI OSTEOGENIK SCAFFOLD KOMPOSIT KITOSAN-GELATIN-KARBONAT APATITBERBASIS BATU KAPUR SEBAGAI KANDIDAT BIOMATERIAL REGENERASI TULANG	Rp 100.000.000
30	Dr. Nurina Fitriani, S.T. Muhammad Fauzul Imron, S.T., M.T. Febri Eko Wahyudianto, ST., MT.	198708122016113201 199408072018083101 199102032016113101	Prof. Madya Ts. Dr. Radin Maya Saphira Binti Radin Mohamed	Alfi Kurnianti INENGAH ILHAM MAULANA	081711133010 081711133031	Hibah Riset Mandat Kolaborasi Mitra Luar Negeri	Sains dan Teknologi	Grup Riset Teknologi dan Inovasi Lingkungan	MODEL SISTEM DINAMIK SARINGAN PASIR SEDERHANA SEBAGAI UPAYA PENYEDIAAN AIR BERSIH DI DAERAH BENCANA	Rp 99.937.000

70	Shofa Aulia Aldhama, S.T., M.T. Chandrawati Putri Wulandari, S.T., M.T., Ph.D.	199407102020013101 199008262020073201	NARESWARI NATHA UDIYANI SAFARDI SAMSA	162012533051 162012533048	Penelitian Dosen Pemula	Teknologi Maju dan Multidisiplin	Human Factor and System Engineering	Analisa Pengaruh Media Consumption dan Anxiety terhadap Kualitas Tidur Tenaga Medis Covid-19	Rp	25,000,000
TOTAL DANA									**Rp**	**1,467,387,900**

Salinan sesuai dengan aslinya
Sekretaris Universitas,

KOKO SRIMULYO
NIP 196602281990021001

Ditetapkan di Surabaya

REKTOR,

TTD

MOHAMMAD NASIH
NIP. 196508061992031002

KEMENTERIAN PENDIDIKAN DAN KEBUDAYAAN
UNIVERSITAS AIRLANGGA
LEMBAGA PENELITIAN DAN PENGABDIAN MASYARAKAT
Kampus C Mulyorejo Surabaya 60115 - Telp. (031) 5995247 Fax. (0315923584)
Website : http://lppm.unair.ac.id; E-mail : penelitian@lppm.unair.ac.id, pengmas@lppm.unair.ac.id

KONTRAK PELAKSANAAN
HIBAH RISET MANDAT KOLABORASI MITRA LUAR NEGERI
UNIVERSITAS AIRLANGGA TAHUN 2021
Nomor : 805/UN3.15/PT/2021

Pada hari ini jumat tanggal dua puluh tiga bulan april tahun dua ribu dua puluh satu, kami yang bertandatangan di bawah ini:

1. Dr. Gadis Meinar Sari, dr., M.Kes. : Ketua Lembaga Penelitian dan Pengabdian Masyarakat Universitas Airlangga yang berkedudukan di Surabaya, dalam hal ini bertindak untuk dan atas nama Rektor Universitas Airlangga; selanjutnya disebut **PIHAK PERTAMA;**

2. Devi Rianti, drg., M.Kes. : Dosen Fakultas Kedokteran Gigi Universitas Airlangga dalam hal ini bertindak sebagai pengusul dan Ketua Pelaksana Penelitian Tahun Anggaran 2021 untuk selanjutnya disebut **PIHAK KEDUA**.

PIHAK PERTAMA dan PIHAK KEDUA secara bersama-sama bersepakat mengikatkan diri dalam suatu Kontrak Pelaksanaan Hibah Riset Mandat Kolaborasi Mitra Luar Negeri Universitas Airlangga Tahun 2021 dengan ketentuan dan syarat-syarat yang diatur dalam pasal-pasal berikut:

PASAL 1
DASAR HUKUM

Kontrak Pelaksanaan Hibah Riset MandatKolaborasi Mitra Luar Negeri Universitas Airlangga Tahun 2021 ini berdasarkan kepada:

1. *Rencana Kegiatan Anggaran Tahunan (RKAT) Lembaga Penelitian dan Pengabdian Masyarakat* Universitas Airlangga Tahun Anggaran 2021;
2. Keputusan Rektor Universitas Airlangga Nomor 212/UN3/2021, tanggal 22 April 2021, tentang Pelaksanaan Penelitian Internal Universitas Airlangga Hibah Riset Mandat Top Tier, Hibah Riset Mandat Kolaborasi Mitra Luar Negeri, Hibah Mandat Article Review, Penelitian Unggulan Fakultas dan Penelitian Dosen Pemula Tahun 2021.

PASAL 2
HAK DAN KEWAJIBAN

(1) PIHAK PERTAMA memberi tugas kepada PIHAK KEDUA, dan PIHAK KEDUA menerima tugas sebagai penanggungjawab pelaksanaan Hibah Riset Mandat Kolaborasi Mitra Luar Negeri Universitas Airlangga Tahun 2021 dengan judul:

" POTENSI OSTEOGENIK SCAFFOLD KOMPOSIT KITOSAN-GELATIN-KARBONAT APATITBERBASIS BATU KAPUR SEBAGAI KANDIDAT BIOMATERIAL REGENERASI TULANG "

(2) PIHAK KEDUA bertanggungjawab penuh dalam pelaksanaan penelitian sebagaimana dimaksud pada ayat (1);

(3) *Pelaksanaan penelitian sebagaimana dimaksud pada ayat (1) wajib menghasilkan luaran* 2 **publikasi** Quartil 3 dalam jangka waktu satu tahun pada Jurnal Ilmiah Internasional terindeks di Scopus

(4) Luaran penelitian sebagaimana tersebut pada pasal 2 ayat (3) mengikuti ketentuan berikut:

a. Penulis pertama (*first author*) dan atau penulis korespondensi (*corresponding author)* pada *setiap publikasi yang dihasilkan adalah salah satu nama dari Tim Peneliti;*
b. Ketua peneliti sekurang-kurangnya menjadi satu sebagai penulis pertama (*first author*) dan atau penulis korespondensi (*corresponding author)* pada publikasi yang dihasilkan ;
c. Anggota peneliti harus tercantum pada sekurang-kurangnya satu publikasi yang dihasilkan.
d. Mitra peneliti asing harus dicantumkan pada publikasi yang dihasilkan
e. Dalam publikasi scopus peneliti wajib mencantumkan salah satu **keyword SDGs, lebih diutamakan untuk menggunakan Fokus SDGs Universitas Airlangga yaitu No Poverty, Good health and well-being, Reduced Inequalities** dan **Partnerships for the goals)**

(5) PIHAK KEDUA wajib melaporkan pelaksanaan penelitian dengan melakukan hal-hal berikut:

a. Mencatat semua kegiatan pelaksanaan penelitian pada Buku Harian Penelitian (*logbook*) *dan mengisi kegiatan harian secara rutin terhitung sejak penandatanganan kontrak;*
b. Menyiapkan bahan pemantauan/monev internal dengan membuat Laporan Kemajuan mengikuti format Panduan Hibah Riset MandatKolaborasi Mitra Luar Negeri dan aturan keuangan yang berlaku;
c. Menyiapkan bahan presentasi monev internal mengikuti format Panduan;
d. Menyiapkan Laporan Akhir penelitian dan mempresentasikannya sebagai pemaparan hasil penelitian;
e. Melaporkan dan menyerahkan bukti luaran penelitian yang dihasilkan serta menyerahkan bukti fisik penggunaan keuangan sebagai pertanggungjawaban keuangan (SPj.)

PASAL 3
JANGKA WAKTU

PIHAK KEDUA *melaksanakan dan menyelesaikan penelitian sebagaimana dimaksud pada Pasal* 2 ayat (1), terhitung mulai tanggal **1 Maret 2021 s.d.** 7 **Desember 2021**.

PASAL 4
CARA PEMBAYARAN

(1) PIHAK PERTAMA memberikan dana untuk kegiatan sebagaimana dimaksud dalam Pasal 2 ayat (1) sebesar **Rp 100.000.000 (Seratus Juta Rupiah),** dibebankan pada Rencana Kegiatan Anggaran Tahunan (RKAT) Lembaga Penelitian dan Pengabdian Masyarakat Universitas Airlangga Tahun Anggaran 2021;

(2) Dana pelaksanaan penelitian ini dibayarkan oleh PIHAK PERTAMA kepada PIHAK KEDUA secara bertahap, dengan ketentuan sebagai berikut:

a) Pembayaran tahap pertama sebesar 70 % dari total bantuan dana yaitu 70% X Rp 100.000.000= **Rp 70.000.000** (Tujuh Puluh Juta Rupiah) dibayarkan oleh PIHAK PERTAMA kepada PIHAK KEDUA setelah penandatanganan kontrak;

b) Pembayaran Tahap Kedua sebesar **30 %** dari total bantuan dana kegiatan yaitu 30% X Rp 100.000.000= **Rp 30.000.000**(Tiga Puluh Juta Rupiah) dibayarkan setelah PIHAK

KEDUA menyelesaikan pekerjaan dan mengunggah semua berkas di *cyber campus*, berupa:

- *Laporan Kemajuan Pelaksanaan Penelitian Dosen Pemula di unggah di cyber campus* paling lambat **15 Agustus 2021**;
- Laporan Akhir Hasil Pelaksanaan Penelitian Dosen Pemula di unggah di *cyber campus* paling lambat **30 November 2021**;
- Artikel Ilmiah berdasarkan Laporan Akhir Penelitian Dosen Pemula;
- Rekapitulasi Keuangan 100% dalam format pdf.
- Laporan/bukti fisik penggunaan keuangan (SPj.) 100% sebanyak satu eksemplar eksemplar paling lambat **7 Desember 2021**;
- Bukti luaran yang dihasilkan berupa paper/Artikel Ilmiah yang telah terpublikasi *(publish/accepted)* di Jurnal Internasional terindeks Scopus paling lambat **17 Agustus 2023**.

(3) Pendanaan **Kontrak Penelitian** sebagaimana dimaksud pada ayat (2) dibayarkan kepada peneliti berdasarkan data sebagai berikut.

Nama Peneliti	:	**Devi Rianti, drg., M.Kes.**
Nomor Rekening	:	**0100891649**
Nama penerima pada rekening	:	**Devi Rianti**
Nama Bank	:	**BNI**
NPWP Perguruan Tinggi	:	**73.773.758.5-619.000**

(4) PIHAK KEDUA bertanggungjawab mutlak dalam pembelanjaan dana tersebut pada ayat (1) sesuai dengan proposal kegiatan yang telah disetujui dan berkewajiban untuk menyampaikan semua bukti-bukti pengeluaran dengan jumlah dana yang diberikan oleh PIHAK PERTAMA.

PASAL 5
PENGGANTIAN KEANGGOTAAN

Apabila PIHAK KEDUA tidak dapat melaksanakan Hibah Riset Mandat Kolaborasi Mitra Luar Negeri, maka PIHAK KEDUA wajib menunjuk pengganti ketua pelaksana Penelitian yang merupakan salah satu anggota tim setelah mendapat persetujuan tertulis dari Ketua Lembaga Penelitian dan Pengabdian Masyarakat Universitas Airlangga;

PASAL 6
SANKSI

(1) Laporan hasil pelaksanaan penelitian sebagaimana dimaksud dalam Pasal 2 ayat (1) harus memenuhi ketentuan sebagaimana tercantum pada Panduan Pelaksanaan Hibah Riset Mandat Kolaborasi Mitra Luar Negeri Universitas Airlangga Tahun 2021;

(2) Apabila sampai dengan batas waktu yang telah ditetapkan PIHAK KEDUA belum menyelesaikan tugasnya dan atau terlambat mengirim laporan Kemajuan dan atau terlambat mengirim laporan Akhir, maka PIHAK KEDUA dikenakan sanksi administratif;

(3) Apabila PIHAK KEDUA tidak dapat memenuhi kewajiban utama di Jurnal Internasional terindeks Scopus sebagaimana dimaksud dalam Pasal 2 ayat (3), maka akan diberikan sanksi mengembalikan dana yang telah diberikan secara proporsional.

(4) Apabila PIHAK KEDUA tidak dapat melaksanakan penelitian ini maka harus mengembalikan dana yang tidak terserap kepada Rektor Universitas Airlangga melalui PIHAK PERTAMA;

(5) Apabila di kemudian hari terbukti bahwa judul Penelitian sebagaimana dimaksud dalam Pasal 2 ayat (1) dijumpai adanya indikasi duplikasi dengan Penelitian lain dan/atau diperoleh indikasi ketidakjujuran/itikad kurang baik yang tidak sesuai dengan kaidah ilmiah, maka kegiatan Penelitian tersebut dinyatakan batal dan PIHAK KEDUA wajib mengembalikan dana seluruhnya Penelitian kepada Rektor Universitas Airlangga melalui PIHAK PERTAMA.

(6) Denda atau pengembalian dana sebagaimana tersebut di atas disetorkan ke Rektor Universitas Airlangga melalui PIHAK PERTAMA;

PASAL 7
PAJAK

PIHAK KEDUA berkewajiban menyetor pajak ke Kantor Pelayanan Pajak setempat yang berkenaan dengan kewajiban pajak berupa :

1. pembelian barang dan jasa dikenai PPN sebesar 10% dan PPh 23 sebesar 2%;
2. pajak–pajak lain sesuai ketentuan yang berlaku;
3. Pajak honorarium untuk non ketua dan non anggota peneliti sebesar 5% untuk yang memiliki NPWP dan 6% untuk yang tidak memiliki NPWP

PASAL 8
KEKAYAAN INTELEKTUAL

(1) Hak Kekayaan Intelektual yang dihasilkan dari pelaksanaan Hibah Riset Mandat Kolaborasi Mitra Luar Negeri ini diatur dan dikelola sesuai dengan peraturan dan perundang-undangan yang berlaku;
(2) Setiap publikasi, makalah, dan/atau ekspos dalam bentuk apapun yang berkaitan dengan hasil penelitian ini wajib mencantumkan **PIHAK PERTAMA** sebagai pemberi dana.
(3) Publikasi tidak boleh *double counting* dengan luaran kegiatan pendanaan penelitian yang lain.
(4) Hasil Hibah Penelitian berupa peralatan dan/atau alat yang dibeli dari kegiatan ini menjadi milik Universitas Airlangga yang dapat dihibahkan kepada institusi/lembaga/masyarakat melalui Berita Acara Serah Terima (BAST).

PASAL 9
PENYELESAIAN PERSELISIHAN

(1) Apabila terjadi perselisihan antara PIHAK PERTAMA dan PIHAK KEDUA dalam pelaksanaan kontrak ini, maka akan dilakukan penyelesaian secara musyawarah untuk mufakat dan apabila tidak tercapai penyelesaian secara musyawarah dan mufakat maka penyelesaian dilakukan melalui proses hukum yang berlaku dengan memilih domisili hukum di Pengadilan Negeri Surabaya;

(2) Hal-hal yang belum diatur dalam perjanjian ini akan diatur kemudian oleh KEDUA BELAH PIHAK.

PASAL 10
KEADAAN MEMAKSA (*FORCE MAJEURE*)

(1) **PARA PIHAK** dibebaskan dari tanggung jawab atas keterlambatan atau kegagalan dalam memenuhi kewajiban yang dimaksud dalam Penugasan Penelitian disebabkan atau diakibatkan oleh peristiwa atau kejadian diluar kekuasaan **PARA PIHAK** yang dapat digolongkan sebagai keadaan memaksa (*force majeure*).

(2) Peristiwa atau kejadian yang dapat digolongkan keadaan memaksa (*force majeure*) dalam Penugasan Penelitian ini adalah bencana alam, wabah penyakit, kebakaran, perang, blokade, peledakan, sabotase, revolusi, pemberontakan, huru hara serta adanya tindakan pemerintah dalam bidang ekonomi dan moneter yang secara nyata berpengaruh terhadap pelaksanaan Penugasan Penelitian ini.

(3) Apabila terjadi keadaan memaksa (*force majeure*) maka pihak yang mengalami wajib memberitahukan kepada pihak lainnya secara tertulis, selambat-lambatnya dalam 7 (tujuh) hari kerja sejak terjadinya keadaan memaksa (*force majeure*), disertai dengan bukti-bukti yang sah dari pihak berwajib, dan **PARA PIHAK** dengan itikad baik akan segera membicarakan penyelesaiannya.

PASAL 11
PENUTUP

Surat Perjanjian Pelaksanaan Hibah Riset Mandat Kolaborasi Mitra Luar NegeriUniversitas Airlangga Tahun 2021 ini dibuat rangkap 2 (dua) bermeterai cukup sesuai dengan ketentuan yang berlaku, dan biaya meterai dibebankan kepada PIHAK KEDUA.

PIHAK KEDUA	**PIHAK PERTAMA**
Devi Rianti, drg., M.Kes.	**Dr. Gadis Meinar Sari, dr., M.Kes.**
NIP. 196309071990022001	**NIP. 196605041996032001**

No : 29/RKMLN/thp-I/2021

SURAT PERTANGGUNGJAWABAN DANA PENELITIAN
UNIVERSITAS AIRLANGGA

Sesuai dengan	:	1. U.U. Nomor 17 Tahun 2003 tentang Keuangan Negara; 2. U.U. Nomor 1 Tahun 2004 tentang Perbendaharaan Negara; 3. U.U. Nomor 20 Tahun 2003 tentang Sistem Pendidikan Nasional; 4. U.U. Nomor 12 Tahun 2012 tentang Pendidikan Tinggi; 5. P.P. Nomor 57 Tahun 1954 tentang Pendirian Universitas Airlangga di Surabaya sebagaimana telah diubah dengan Peraturan Pemerintah nomor : 3 Tahun 1955 tentang pengubahan Peraturan Pemerintah Nomor : 1954; 6. P.P. Nomor 37 Tahun 2009 tentang Dosen; 7. P.P. Nomor 30 Tahun 2014 tentang Statuta Universitas Airlangga; 8. Peraturan Wali Amanat Universitas Airlangga.
Unit Kerja	:	2 0 2 0 0 Lembaga Penelitian Dan Pengabdian Masyarakat Universitas Airlangga
Kode Kegiatan	:	
Kode Rekening	:	

Telah Terima	:	Rektor Universitas Airlangga
Terbilang Rp.	:	Tujuh Puluh Juta Rupiah
Untuk Pembayaran	:	Program Penelitian Hibah Riset Mandat Kolaborasi Mitra Luar Negeri Universitas Airlangga Tahun 2021
Judul	:	POTENSI OSTEOGENIK SCAFFOLD KOMPOSIT KITOSAN-GELATIN-KARBONAT APATITBERBASIS BATU KAPUR SEBAGAI KANDIDAT BIOMATERIAL REGENERASI TULANG
Sumber Dana	:	Universitas Airlangga Tahun Anggaran 2021
Termin	:	I
Ketua Peneliti	:	Devi Rianti, drg., M.Kes.
Jumlah	:	**Rp. 70.000.000**

Surabaya, 23 April 2021

Lunas Dibayar Bendahara

Ketua Peneliti

Wishnu Okky Pranadi Tirta
NIP. 199210232018013101

Devi Rianti, drg., M.Kes.
NIP. 196309071990022001

Mengetahui / Menyetujui
Atasan Langsung Bendahara

Dr. Gadis Meinar Sari, dr., M.Kes.
NIP. 196605041996032001

No : 29/RKMLN/thp-I/2021

SURAT PERTANGGUNGJAWABAN DANA PENELITIAN
UNIVERSITAS AIRLANGGA

Sesuai dengan	:	1. U.U. Nomor 17 Tahun 2003 tentang Keuangan Negara; 2. U.U. Nomor 1 Tahun 2004 tentang Perbendaharaan Negara; 3. U.U. Nomor 20 Tahun 2003 tentang Sistem Pendidikan Nasional; 4. U.U. Nomor 12 Tahun 2012 tentang Pendidikan Tinggi; 5. P.P. Nomor 57 Tahun 1954 tentang Pendirian Universitas Airlangga di Surabaya sebagaimana telah diubah dengan Peraturan Pemerintah nomor : 3 Tahun 1955 tentang pengubahan Peraturan Pemerintah Nomor : 1954; 6. P.P. Nomor 37 Tahun 2009 tentang Dosen; 7. P.P. Nomor 30 Tahun 2014 tentang Statuta Universitas Airlangga; 8. Peraturan Wali Amanat Universitas Airlangga.
Unit Kerja	:	2 0 2 0 0 Lembaga Penelitian Dan Pengabdian Masyarakat Universitas Airlangga
Kode Kegiatan	:	
Kode Rekening	:	

Telah Terima	:	Rektor Universitas Airlangga
Terbilang Rp.	:	Tujuh Puluh Juta Rupiah
Untuk Pembayaran	:	Program Penelitian Hibah Riset Mandat Kolaborasi Mitra Luar Negeri Universitas Airlangga Tahun 2021
Judul	:	POTENSI OSTEOGENIK SCAFFOLD KOMPOSIT KITOSAN-GELATIN-KARBONAT APATITBERBASIS BATU KAPUR SEBAGAI KANDIDAT BIOMATERIAL REGENERASI TULANG
Sumber Dana	:	Universitas Airlangga Tahun Anggaran 2021
Termin	:	I
Ketua Peneliti	:	Devi Rianti, drg., M.Kes.
Jumlah	:	**Rp. 70.000.000**

Surabaya, 23 April 2021

Lunas Dibayar Bendahara

Wishnu Okky Pranadi Tirta
NIP. 199210232018013101

Ketua Peneliti

Devi Rianti, drg., M.Kes.
NIP. 196309071990022001

Mengetahui / Menyetujui
Atasan Langsung Bendahara

Dr. Gadis Meinar Sari, dr., M.Kes.
NIP. 196605041996032001

No : 29/RKMLN/thp-II/2021

SURAT PERTANGGUNGJAWABAN DANA PENELITIAN
UNIVERSITAS AIRLANGGA

Sesuai dengan	:	1. U.U. Nomor 17 Tahun 2003 tentang Keuangan Negara; 2. U.U. Nomor 1 Tahun 2004 tentang Perbendaharaan Negara; 3. U.U. Nomor 20 Tahun 2003 tentang Sistem Pendidikan Nasional; 4. U.U. Nomor 12 Tahun 2012 tentang Pendidikan Tinggi; 5. P.P. Nomor 57 Tahun 1954 tentang Pendirian Universitas Airlangga di Surabaya sebagaimana telah diubah dengan Peraturan Pemerintah nomor : 3 Tahun 1955 tentang pengubahan Peraturan Pemerintah Nomor : 1954; 6. P.P. Nomor 37 Tahun 2009 tentang Dosen; 7. P.P. Nomor 30 Tahun 2014 tentang Statuta Universitas Airlangga; 8. Peraturan Wali Amanat Universitas Airlangga.
Unit Kerja	:	2 0 2 0 0 Lembaga Penelitian Dan Pengabdian Masyarakat Universitas Airlangga
Kode Kegiatan	:	
Kode Rekening	:	

Telah Terima	:	Rektor Universitas Airlangga
Terbilang Rp.	:	Tiga Puluh Juta Rupiah
Untuk Pembayaran	:	Program Penelitian Hibah Riset Mandat Kolaborasi Mitra Luar Negeri Universitas Airlangga Tahun 2021
Judul	:	POTENSI OSTEOGENIK SCAFFOLD KOMPOSIT KITOSAN-GELATIN-KARBONAT APATITBERBASIS BATU KAPUR SEBAGAI KANDIDAT BIOMATERIAL REGENERASI TULANG
Sumber Dana	:	Universitas Airlangga Tahun Anggaran 2021
Termin	:	II
Ketua Peneliti	:	Devi Rianti, drg., M.Kes.
Jumlah	:	**Rp. 30.000.000**

Lunas Dibayar Bendahara

Wishnu Okky Pranadi Tirta
NIP. 199210232018013101

Surabaya, 23 April 2021
Ketua Peneliti

Devi Rianti, drg., M.Kes.
NIP. 196309071990022001

Mengetahui / Menyetujui
Atasan Langsung Bendahara

Dr. Sadis Meinar Sari, dr., M.Kes.
NIP. 196605041996032001

No : 29/RKMLN/thp-II/2021

SURAT PERTANGGUNGJAWABAN DANA PENELITIAN
UNIVERSITAS AIRLANGGA

Sesuai dengan	:	1. U.U. Nomor 17 Tahun 2003 tentang Keuangan Negara; 2. U.U. Nomor 1 Tahun 2004 tentang Perbendaharaan Negara; 3. U.U. Nomor 20 Tahun 2003 tentang Sistem Pendidikan Nasional; 4. U.U. Nomor 12 Tahun 2012 tentang Pendidikan Tinggi; 5. P.P. Nomor 57 Tahun 1954 tentang Pendirian Universitas Airlangga di Surabaya sebagaimana telah diubah dengan Peraturan Pemerintah nomor : 3 Tahun 1955 tentang pengubahan Peraturan Pemerintah Nomor : 1954; 6. P.P. Nomor 37 Tahun 2009 tentang Dosen; 7. P.P. Nomor 30 Tahun 2014 tentang Statuta Universitas Airlangga; 8. Peraturan Wali Amanat Universitas Airlangga.
Unit Kerja	:	2 0 2 0 0 Lembaga Penelitian Dan Pengabdian Masyarakat Universitas Airlangga
Kode Kegiatan	:	
Kode Rekening	:	

Telah Terima	:	Rektor Universitas Airlangga
Terbilang Rp.	:	Tiga Puluh Juta Rupiah
Untuk Pembayaran	:	Program Penelitian Hibah Riset Mandat Kolaborasi Mitra Luar Negeri Universitas Airlangga Tahun 2021
Judul	:	POTENSI OSTEOGENIK SCAFFOLD KOMPOSIT KITOSAN-GELATIN-KARBONAT APATITBERBASIS BATU KAPUR SEBAGAI KANDIDAT BIOMATERIAL REGENERASI TULANG
Sumber Dana	:	Universitas Airlangga Tahun Anggaran 2021
Termin	:	II
Ketua Peneliti	:	Devi Rianti, drg., M.Kes.
Jumlah	:	**Rp. 30.000.000**

Surabaya, 23 April 2021
Ketua Peneliti

Materai Rp. 10.000

Devi Rianti, drg., M.Kes.
NIP. 196309071990022001

Lunas Dibayar Bendahara

Wishnu Okky Pranadi Tirta
NIP. 199210232018013101

Mengetahui / Menyetujui
Atasan Langsung Bendahara

Dr. Gadis Meinar Sari, dr., M.Kes.
NIP. 196605041996032001

Original article

Institution of MECHANICAL ENGINEERS
Journal of MATERIALS: DESIGN AND APPLICATIONS

Proc IMechE Part L:
J Materials: Design and Applications
1–14

DOI: 10.1177/14644207221080115
journals.sagepub.com/home/pil
SAGE

Influence of bone marrow characteristic and trabecular bone morphology on bone remodelling process with FSI approach

AAR Rabiatul[1], Devi Rianti[2], SJ Fatihhi[3], Amir Putra Md Saad[4], Zulfadzli Zakaria[1], Anita Yuliati[3], MN Harun[2,5], MRA Kadir[5,6], Andreas Öchsner[7], Tunku Kamarul[8], Khalid M Saqr[9] and Ardiyansyah Syahrom[1,2]

Abstract

While doing daily physiological activities, the trabecular bone will experience a certain amount of deformation which leads to the bone marrow movement. The movement can affect the bone remodelling process and the properties of the bone itself. The bone marrow plays a role as a hydraulic stiffening of the trabecular structure. However, previous studies analysed on trabecular bone and bone marrow separately, which is not considered as the actual condition. Thus, it is crucial to consider combine analyses of the bone marrow with the trabecular structure simultaneous. The aim of this study is to investigate the effect of bone marrow on the mechanical environment and the structure of trabecular bone during normal walking loading. Hence, this study used the Fluid-Structure Interaction (FSI) approach as a finite element method to discover the effect of bone marrow to the trabecular structure and vice versa. The findings show the shear stress value along normal walking phase was found in a range of 0.01–0.27 Pa which is sufficient to regulated cell response minimally. This study provides insight into understanding the related mechanobiological responds towards supply of nutrients onto bone cells.

Keywords

Fluid Structure Interaction, Trabecular Bone, Bone Marrow, Shear Stress, Stiffness, Bone Remodelling

Date received: 10 October 2021; final manuscript received January 27, 2022; accepted: 27 January 2022

Introduction

Physiological loading induced trabecular bone deformation that leads to the bone marrow movement within the porous structure which contribute to stimulating the osteogenic response to the bone cells.[1] The forces from the physiological loading cause both small strain and shear stress which known as a key to initiate the bone remodelling process.[2–5] Currently, researchers tried to discover the actual value necessary to stimulate the bone cells for the bone remodelling process. To this date, experimental and simulation study have been performing in order to capture the value of these biomechanical stimuli that encourage the remodelling process.[6–8] Bone marrow is a

[1]Medical Device Technology Center (MEDiTEC), Institute Human Centred Engineering (iHumEn), Universiti Teknologi Malaysia, Johor, Malaysia
[2]Dental materials science Department, Faculty of Dentistry Medicine, Universitas Airlangga, Surabaya, Jawa Timur, Indonesia
[3]Universiti Kuala Lumpur, Malaysian Institute of Industrial Technology, Kuala Lumpur, Malaysia
[4]School of Mechanical Engineering, Faculty of Engineering, Universiti Teknologi Malaysia, Johor, Malaysia
[5]Sports Innovation and Technology Centre (SITC), Institute Human Centred Engineering (iHumEn), Universiti Teknologi Malaysia, Johor, Malaysia
[6]School of Biomedicals Engineering and Health Sciences, Faculty of Engineering, Universiti Teknologi Malaysia, Johor, Malaysia
[7]Lightweight Design / Structural Simulation, Faculty of Mechanical Engineering, Esslingen University of Applied Sciences, Esslingen, Germany
[8]Tissue Engineering Group (TEG), National Orthopaedic Centre of Excellence in Research and Learning (NOCERAL), Department of Orthopaedic Surgery, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia
[9]College of Engineering and Technology, Arab Academy for Science, Technology and Maritime Transport, Alexandria, Egypt

Corresponding authors:
Ardiyansyah Syahrom, Medical Device Technology Center (MEDiTEC), Institute Human Centred Engineering (iHumEn), Universiti Teknologi Malaysia, Skudai, 81300, Malaysia.
Email: ardiyans@gmail.com

Devi Rianti, Dental materials science Department, Faculty of Dentistry Medicine, Universitas AirlanggaSurabaya, Jawa Timur, Indonesia.
Email: devi-r@fkg.unair.ac.id

prime component in trabecular bone, in which it accommodates bone predecessors' cells for bone remodelling. Thus, it is important to consider it presence to better represent the actual conditions of trabecular bone. Therefore, knowledge of biomechanical environment that occur within the trabecular bone during daily physiological activities is necessary to comprehend on how the bone marrow can affect the bone remodelling.

Physiological loading includes daily activities such as house chores, daily walking, and sports activity helps in maintaining the bone health by transferring force to the bone structure. These can be seen on immobilization and bedrest individual that had reduce in their bone mass.[9,10] These relationship of loading and bone formation had been support with the Wolff's law since 1892.[11] The trabecular bone experience compression and tension in the microstructure due to the loading causing the micro strain which one of the mechanical stimuli. Previous study reported that the physiological activities initiate in range of 0.001–0.003 mm/mm on the trabecular structure.[12,13] However, minimal physiological activity cause 1000με which cause bone resorption process higher compare to the bone resorption.[14] Amazingly the bone can heal itself when there is external loads act upon the cells which can help in cells excite by signalling to the bones to start building themselves up. Then again, the loads from human daily life will also initiate the movement of bone marrow within the structure which cause the shear stress that act as response to the remodelling process.[15]

The osteogenic response include osteoprogenitor cells secrete autocrine factors, for example prostaglandins E_2 (PGE_2) and nitric oxide (NO), which can regulate the remodelling activity.[16] In addition, the proliferation rates have been found increasing when the bone marrow stromal cells were exposed to the fluid flow, which means higher number of cells participate in bone formation.[17] The mesenchymal stem cells (MSCs) has been actively investigate in experiment and simulation due to its ability to differentiate into other cells such as osteoblast (bone cells), chondrocytes (cartilage cells) and adipocytes (fat cells).[18–20] The shear stress known as one of the parameters required for the MSCs in the bone marrow to differentiate and assists the remodelling activity.[20,21] The range of shear stress need for the cells to response mention by previous study is about 0.02 to 1.0 Pa.[2,22–25] Undoubtedly, bone remodelling process also requires adequate nutrient transport through the bone cells. These were also with help of bone marrow which function to transport the nutrient and remove waste. However, knowledge on how shear stress value contributing in MSCs to differentiate to different cells are still shallow.

In the present work the movement of the bone marrow regulate osteogenic responds which relate to the trabecular bone deformation due to the physiological activity. Thus far, the is no study using physiological gait loading as boundary to examine the effect of interaction on mechanical stimulus and trabecular bone. Therefore, the aim of this study is to investigate the effect of bone marrow mechanical environment and trabecular bone structure during normal walking loading. A fluid structure interaction (FSI) approach was applied to determine the deformation of trabecular bone with corresponding of marrow shear stress in bone remodelling activity.

Materials and methods

Sample preparation

The fresh bovine femur bones were harvested from the local slaughterhouse and kept frozen at −18°C to 26°C. Specimens of trabecular bone were taken by using a Bosch circular saw with copious water irrigation. The femur bone was then divided and cut into a section of medial condyle, femoral neck and femoral ball with the vertical orientation due to the maximum extension of knee joint occurred. The trabecular bone was then again cut into a cubic shape (10mm × 10mm × 17mm) in length by using a precision cutting tool (Allied Techcut, USA). The precision cutter consists of diamond-resin bonded wafering blade with a minimum speed of 150–250 rpm with continuously water irrigation to prevent heat-related damages. Then, the specimens were placed in small airtight plastic bag with the purpose of reducing the thermal cycling and stored in the freezer with a temperature below −26°C. After that, the specimens will go through next procedure using the ultrasonic cleaner (Crest ultrasonic, model P11000SR, USA) additional with a chemical detergent (Pumicizedcitrius, Gent-l-kleen,USA) to cleaned from marrow. The specimens were then submerged for about 10–15 min at a temperature below 46°C. In order to remove the loose particles and excessive marrow, the specimens were then air-jetted and vacuumed suction. This procedure was repeated until all excessive marrow is removed (Fatihhi SJ et al. 2015). A custom jig was used to align the specimen for improved vertical oriented. Afterwards, the specimens sealed in an airtight bag placed in a −20° C freezer and frozen overnight while the adhesive completely cured. Only then, the samples are scan by using the μ-CT scanner (SkyScan 1172, Bruker MicroCT, Belgium).

Model development

The two-dimensional image data sets from the μ-CT scan were stacked in sequence by Mimics software (MIMICS 12, Materialise, Belgium) and converted into rectangular shape to construct the trabecular model. The thickness of each images slice is 15 μm. The stacked image datasets were calculated into three-dimensional trabecular model through image segmentation by the Mimics software. Subsequently, the image datasets were thresholded to select the region of interest for three-dimensional constructed model. In addition, by using an adapted marching cubes algorithm, the triangular surface meshes were generated for the trabecular model. Then again, the result of triangular surface mesh was very fine, which needed to follow with step of removing noise, redundant parts and irregularities

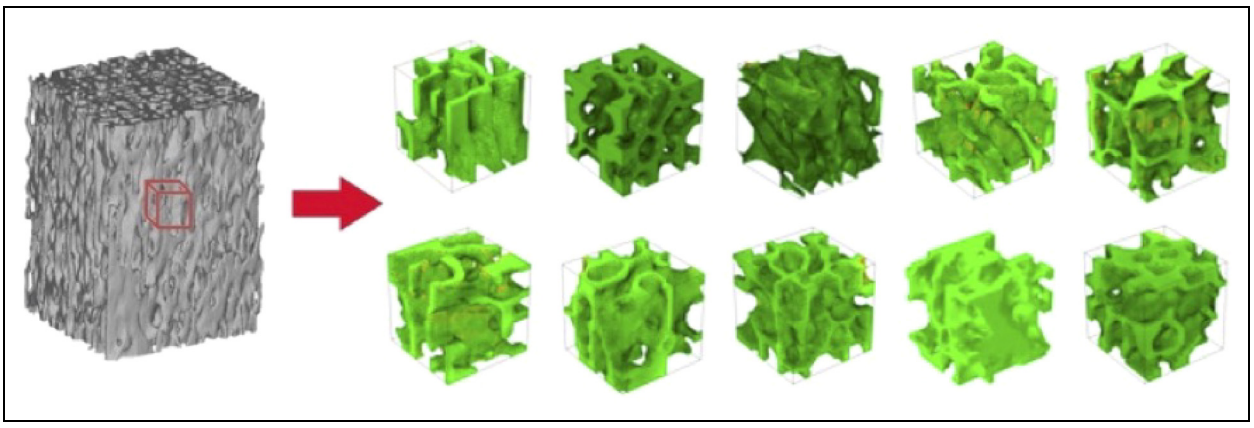

Figure 1. Development of three-dimensional model into sub volume model.

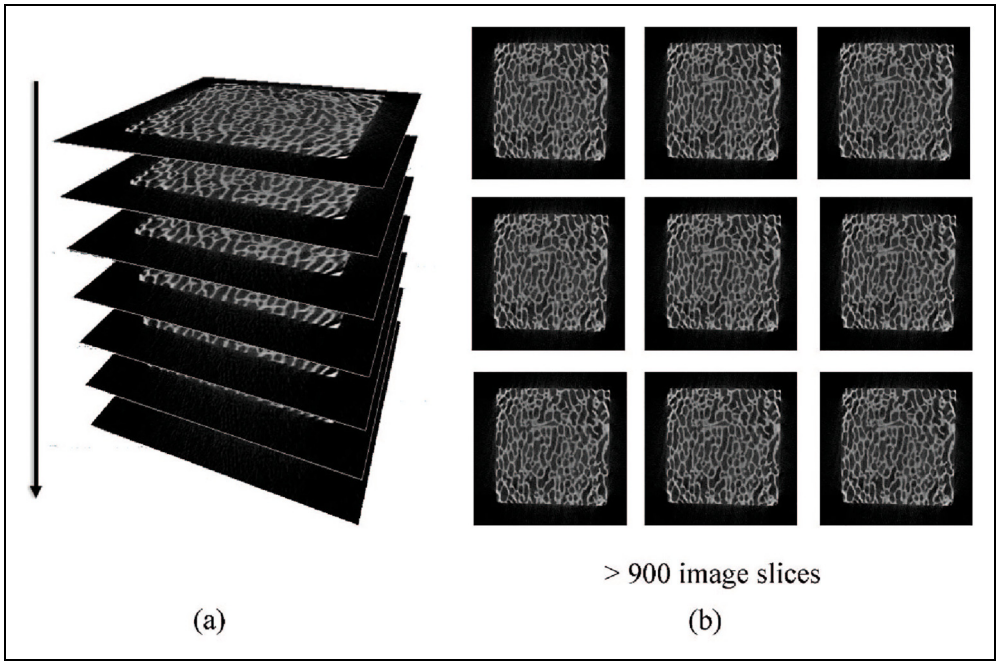

Figure 2. Images obtain from μ-CT scan with (a) images stacked in sequence according to sample orientation (b) raw scanned images file.

shape to construct accurate three-dimensional models. There were 10 models generated and tested in this study.

As for finite element analysis simulation, small sized sub volume region of interest was selected from the fine mesh trabecular bone constructed models (Figure 1) due to the limitation of computer capability to complete the simulation study. These models were then converted into finite element mesh for the simulation. In addition, the trabecular bone model surface meshes with jagged or bad sector are also repaired before importing the model. For the FSI study purpose, the outer wall of the models needed to convert into a flat surface. Thus, for the model preparation, the smaller size sub-models were then merged with cube surface mesh in the Mimics software. After that, the uneven surface of trabecular sub volume models was removed according to the sub volume model shape. Then, the space between the sub model and the cube were stitch together by creating a triangular mesh in between the space. These steps were applied to all six surfaces for the sub trabecular model. Finally, the surface mesh is exported to an STL format file.

Morphology study. From the μ-CT scan images, the morphological study was conducted. One of a trabecular bone sample contains approximately 900 image slices (Figure 2 (b)). The morphological indices were measured using ImageJ (ImageJ, National Institute of Health, USA). All these slices were import and stacked (Figure 2 (a)) by using BoneJ plugins in ImageJ software to obtain the trabecular morphological data. The parameters measured included BV/TV, Tb.Th, Tb.Sp, Tb.N, DA, MIL, etc. All data present in Table 1.

Table 1. Morphological indices of trabecular bone sample.

Parameter	Minimum	Maximum	Mean	SD
BV/TV	0.318	0.477	0.379	0.057
Tb.Th (mm)	0.128	0.559	0.207	0.057
Tb.Sp (mm)	0.253	1.022	0.441	0.137
BS/BV	11.313	15.857	13.677	1.719
DA	0.38	0.684	0.611	0.146
Conn.D (mm^{-3})	19.625	59.875	37.975	14.179
SMI	0.875	1.918	1.416	0.316
Porosity (%)	62	76	70	5
Bone Surface Area (mm^2)	28.802	37.518	32.447	3.134

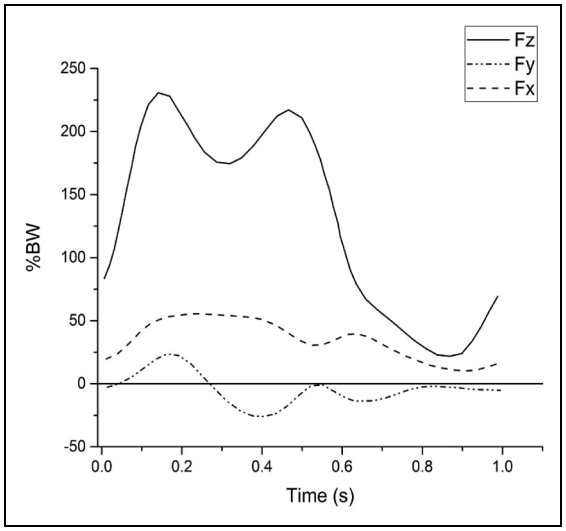

Figure 3. Gait loading of normal walking based on body weight percentage (bergmann G. *et al*., 2001).

Computational simulation

Two-way fluid-structure analysis were conducted using COMSOL Multiphysics software with purpose of investigate the fluid behaviour of bone marrow under gait loading conditions. A gait loading which representing normal walking were applied through the cap faces feature which considered as a rigid body. The gait loading (Figure 3) applied in multi-axis according to normal walking phase.[26] The normal walking phase of gait cycle was divided into 40 discrete points for the simulation. The cap faces feature is vital in the FSI study due to restriction coupling between the trabecular model and marrow model within the FEA. In addition, the prescribed displacement was applied to the cap, where the domain was restricted in the X and Y directions (Figure 4). As for the fluid boundary, the plane of the bottom boundary of fluid was applied as symmetry in order to ensure that the marrow volume remains within the domain when there is load applied through the structure. Moreover, in order to prevent normal velocity to the respective boundary, the marrow flow was model as symmetric in their normal directions. The convergence analysis in this study conclude that 400 thousand tetrahedral elements and shape function was used tessellation method is Delaunay on average were needed for accurate result computation (see Figure 5). In addition, the FSI interface uses an arbitrary Lagrangian-Eulerian (ALE) method, which allows moving boundaries without the need for the mesh movement to follow the material. This ALE method combined the fluid flow formulated using a Eulerian description and a spatial frame with solid mechanics formulated using a Lagrangian description and a material frame. The analysis was performed with the criterion of the von Mises stress criterion less than 5%.

The time-dependent solution is obtained for every gait cycle. Details on the force parameters implemented in this study was demonstrated in.[27] The solid trabecular structures were modelled as a linear elastic material.[28] An elastic modulus (E) of 1000 MPa[29] and Poison's ratio of 0.3 was attributed to the trabecular bone solid structure.[30] Additionally, the viscosity of fluid marrow was assigned 0.4 Pa.s and modelled as incompressible according to Bryant et al.'[31] Newtonian fluid with density of 1060 kg/m^3.[32] The surface between the trabecular structure and marrow fluid is assigned as no-slip boundary.

In the present work, the bone marrow was modelled as an incompressible liquid. The incompressible Navier-Stokes equation was considered as the governing equation, in which;

$$\nabla \cdot u_{fluid} = 0 \tag{1}$$

On the other hand, the momentum equation was as follows;

$$\rho \frac{\partial u_{fluid}}{\partial t} + \rho(u_{fluid} \cdot \nabla)u_{fluid} = \nabla \cdot [-pI + \mu(\nabla u_{fluid} + (\nabla u_{fluid})^T)] + F \tag{2}$$

where the external force acting on the fluid was denoted by **F**, and gravity was neglected. Meanwhile, equation for solid at local equilibrium is given by;

$$\rho \frac{\partial^2 u_{solid}}{\partial t^2} - \nabla \cdot \sigma = F_v \tag{3}$$

where σ and F_v are the Cauchy stress tensor and body force, respectively. Deformed structure was demonstrated by u_{solid}, whereas the Piola-Kirchhoff stress, S was used to calculate the Cauchy stress using the following equation;

$$\sigma = J^{-1}\,\mathrm{FS}\mathrm{F}^{\mathrm{T}}. \tag{4}$$

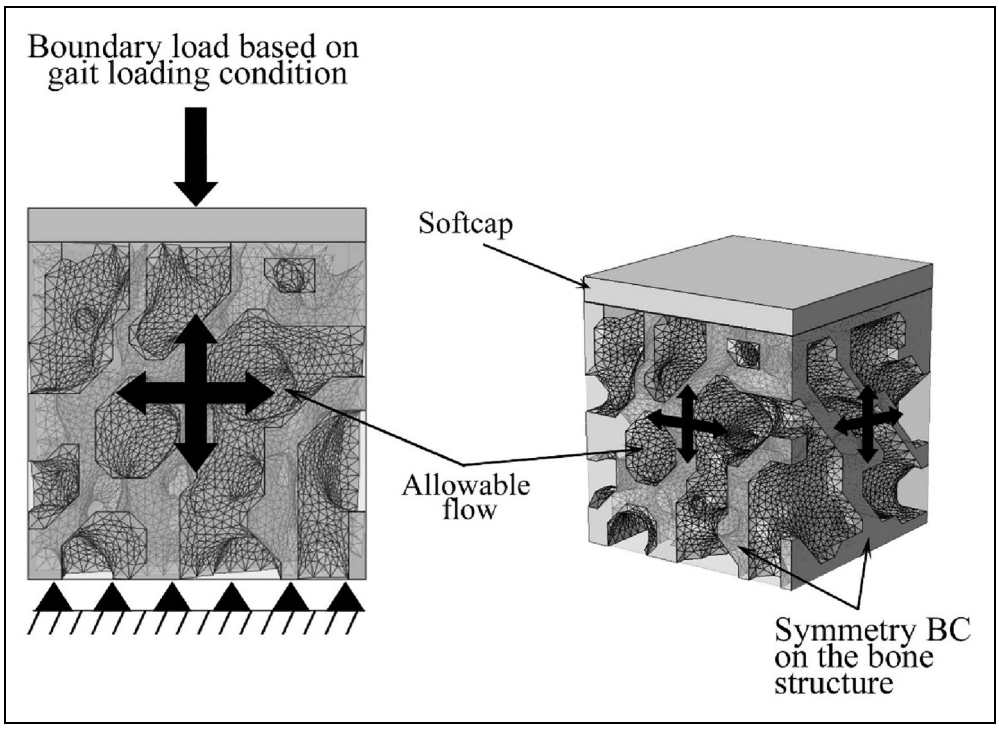

Figure 4. Boundary conditions (BC) of trabecular bone and bone marrow models.

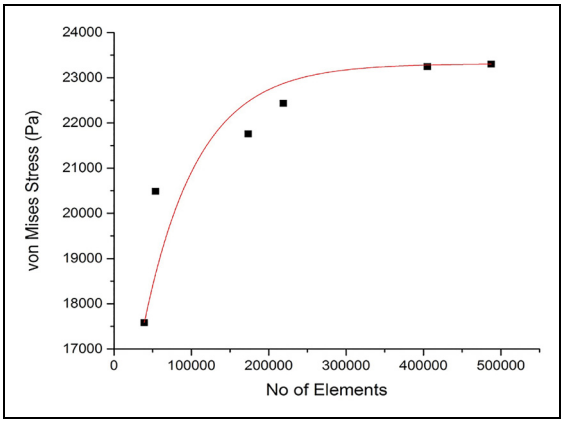

Figure 5. Convergence study for the trabecular structure model.

Using the gradient of displacement vector u_{solid}, the deformation gradient, **F** can be expressed as;

$$F = (I + \nabla u_{solid}), \tag{5}$$

In which the identity matrix was denoted by **I**, and the Jacobian of the deformation is defined as;

$$J = \det(F). \tag{6}$$

Fluid domain was solved based on Eulerian formulation, while solid domain was solved based on Langrangian formulations. In coupling fluid-solid system, the arbitrary Lagrangian-Eularian method can be implemented with total force on the fluid-solid boundary was given as;

$$f_r = n \cdot [-pI + \mu(\nabla u_{fluid} + (\nabla u_{fluid})^T)], \tag{7}$$

With **n** is the normal acting outward at the boundary, the force at the structure's boundary is given by;

$$F_r = \boldsymbol{\sigma} \cdot \boldsymbol{n}. \tag{8}$$

In Spatial and material coordinate system, these forces can be coupled thru a force transformation using the arbitrary Eulerian-Lagrangian method as follows:

$$F_r = f_r \cdot \frac{dv}{dV}\ . \tag{10}$$

Mesh element scale factors dv and dV are the fluid and material frames, respectively. Further, the relationship of structural velocity of the moving wall with the fluid velocity is demonstrated as follows:

$$u_{fluid} = u_w, \tag{11}$$

Thus, the rate of change of the solid displacement is defined by the structural velocity.

$$u_w = \frac{\partial u_{solid}}{\partial t} \tag{12}$$

Statistical analysis

All morphology indices are presented in mean and standard deviation (Table 1). The Pearson's correlation and linear regression analysis were performed to explore the interrelationship between the morphological indices and the mechanical properties of the trabecular bone sample. The multiple linear regression was perform using IBM SPSS Statistics 23 (IBM Corp, USA). For all comparison, the level of significant for p-value was <0.05.

Results

The average von Mises stress distribution during normal walking with cycle duration was plotted as shown in Figure 6. The peak pressure reached as high as 11.35×10^5 Pa. Then again, the minimum stress for trabecular bone is 10.75×10^4 Pa at period of 0.86s. As can be seen, the behaviour of von Mises stress during gait cycle is similar to the force in the vertical direction. From the computational FSI simulation, the von Mises stress distribution within the trabecular bone model along gait normal walking gait loading cycle at different time frame as illustrated in Figure 7. Comparing Figure 7(a) and (b), more area covered with high stresses at time 0.14 s. These results match with the graph of the von Mises stress over time.

The pressure and shear stress distribution during gait loading cycle are presented in Figure 8. This figure shows how the structure of trabecular bone affects the fluid characteristic during the gait loading cycle. It can be observed from the Figure 8 that the pattern of pressure distribution was similar to the von Mises stress results. The pressure was range from 380 to 4070 Pa during the normal walking cycle. Moreover, as discussed earlier, the trabecular structure experience shear stress due to bone marrow movement. With an average of 0.09 Pa, the shear stress was in the range of 0.01 to 0.27 Pa.

Based on 2D images of the trabecular model cross section, the pressure on top section was lower than below section when the structure at the highest compression deformation Figure 9(a). However, at period 0.86 s, the pressure on top section becomes higher than the

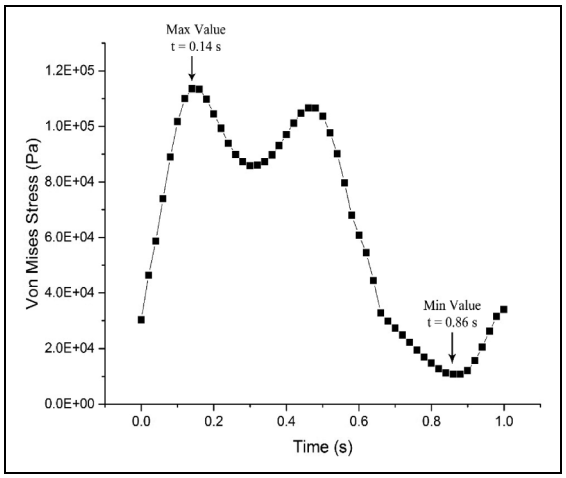

Figure 6. Von Mises stress distribution on the trabecular bone during normal walking.

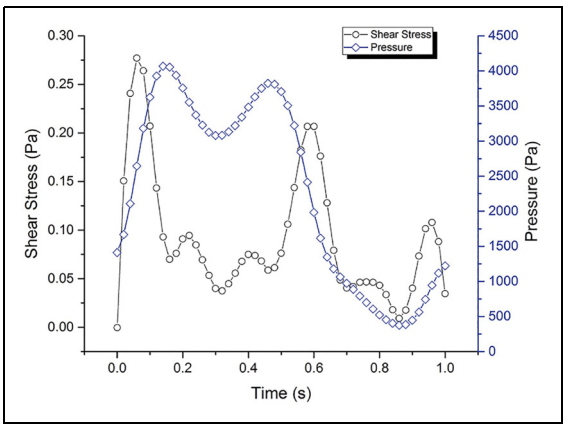

Figure 8. Maximum shear stress and pressure distribution on the trabecular bone along with normal walking loading.

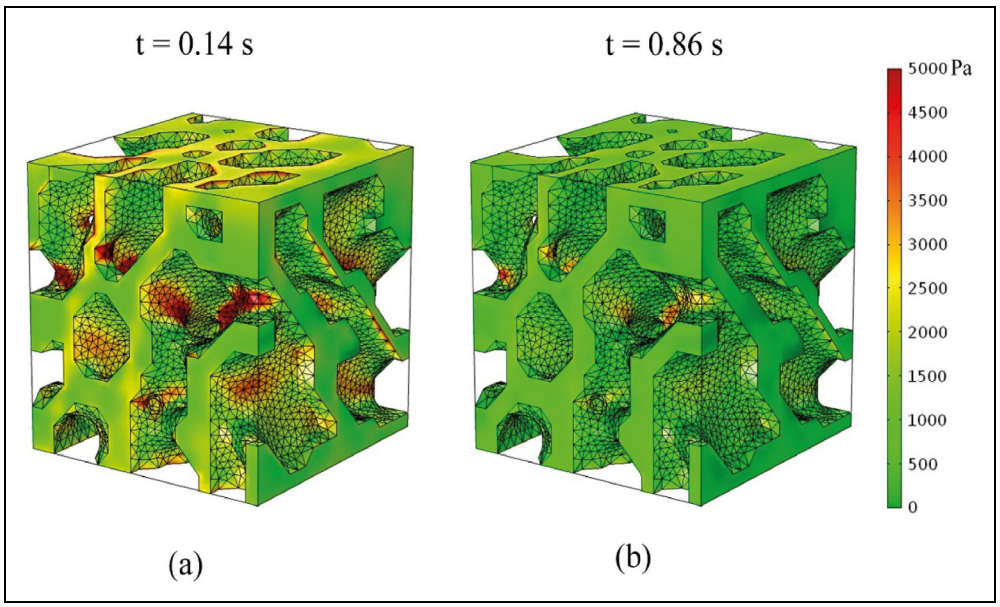

Figure 7. Comparison of von Mises stress on the trabecular bone at different time frame (a) t = 0.14 s and (b) t = 0.86 s.

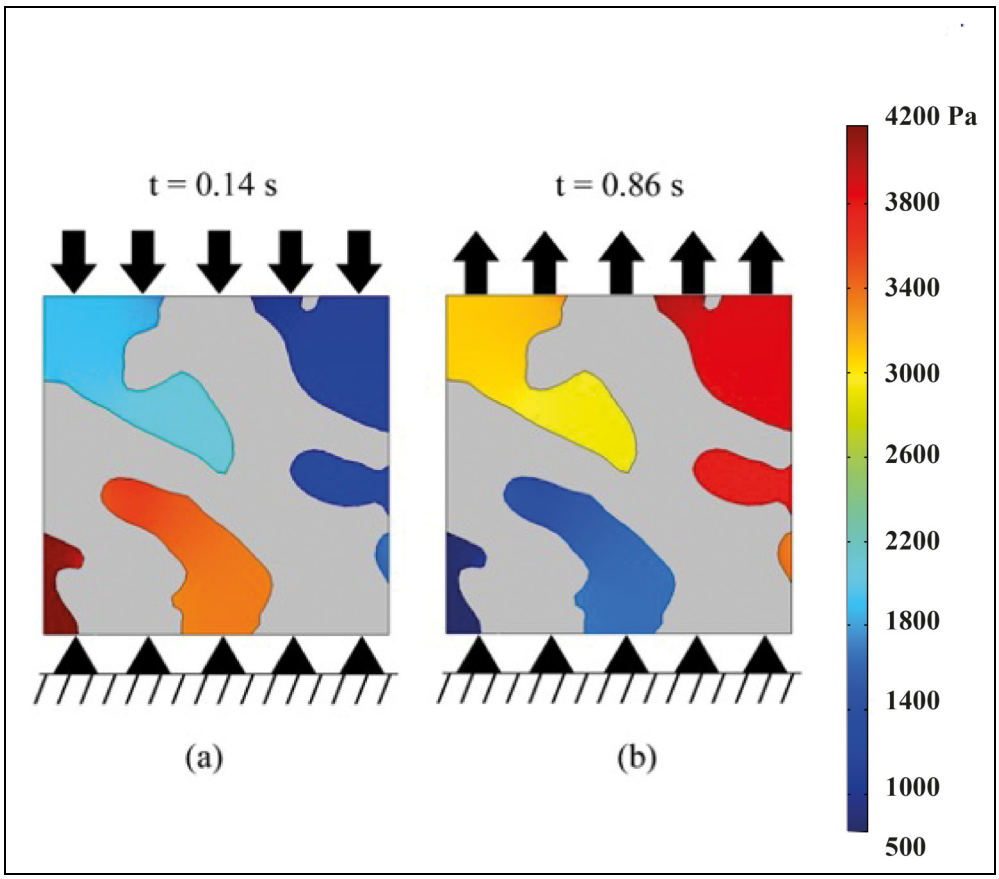

Figure 9. Comparison of pressure distribution on the trabecular bone cross section at different time frame (a) t = 0.14 **s** and (b) t = 0.86 s.

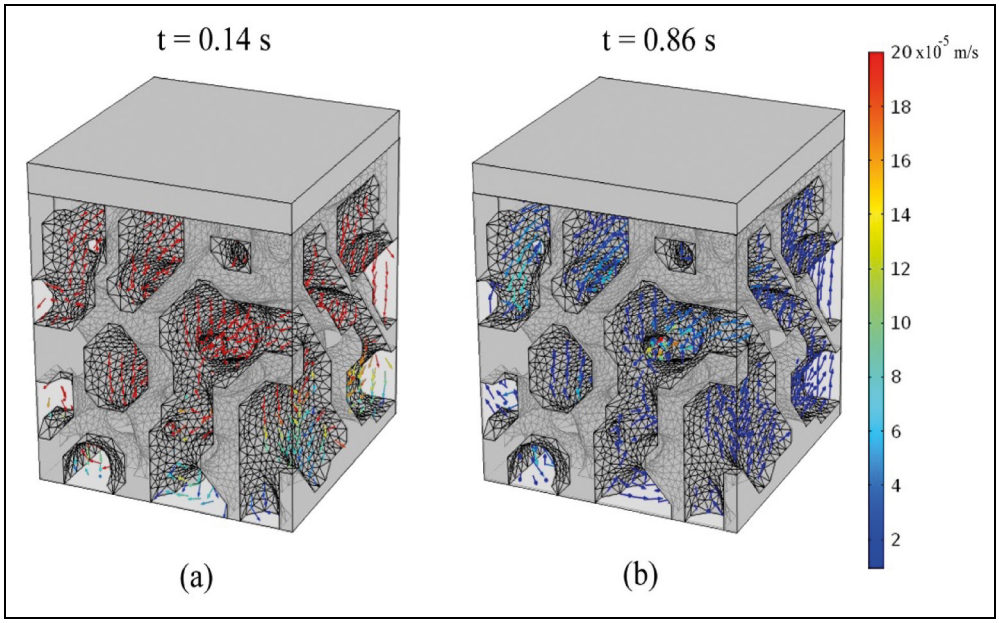

Figure 10. Velocity profile on the trabecular bone at different time frame (a) t = 0.14 s and (b) t = 0.86 s during normal gait loading.

lower section. Figure 10 shows velocity profile of marrow during gait loading cycle at different time frame. As can be seen, at period 0.14s, the velocity was higher than at period 0.86 s. The velocity was range of 0.09 μm/s to 81.2 μm/s at period of 0.14 s and 0.001 μm/s to 2.6 μm/s at period 0.86 s.

Multiple regression analysis for morphological parameters is tabulated in Table 2 and Table 3 with Pearson

correlation and *p*-value for solid and fluid characteristic. Bone volume fraction and SMI shows good correlation with principal strain and von Mises stress. However, the SMI value only significant with principal strain and bone volume fraction solitary shows significant value with von Mises stress. As for marrow characteristic, velocity and pressure were significant to SMI, while shear stress is insignificant with all morphological parameters.

The volume fraction plays a major role in trabecular bone mechanical properties. The distribution of von Mises stress on different model with different bone volume fraction is shown in Figure 11. As can be seen, low bone volume fraction model result in higher von Mises stress compare with a model which has high volume fraction.

The permeability and trabecular stiffness relationship to bone volume fraction and SMI are plotted in Figure 12. The graph showed a strong and negative correlation between the permeability and bone volume fraction ($r = -0.862$), whereas the correlations are strong and positive between permeability and SMI ($r = 0.835$). Meanwhile, in Figure 13 shows both bone volume fraction and SMI have a strong correlation with the trabecular stiffness ($r = 0.832$ and $r = -0.796$; respectively). However, the trabecular bone stiffness correlation was inversely compared to the permeability.

Table 2. Morphological parameters of trabecular bone sample with Pearson correlation and p-value in relation with mechanical behaviour.

	Principle Strain		Von Mises Stress	
Morphological Parameters	Pearson Correlation	*p*-value	Pearson Correlation	*p*-value
BV/TV	−0.830	0.123	−0.798	0.006*
BS/TV	0.449	0.452	0.28	0.132
SMI	0.850	0.002*	0.715	0.689
Conn. D	−0.032	0.916	−0.303	0.16
Tb.Th	−0.426	0.566	−0.344	0.206
Tb.Sp	0.705	0.403	0.769	0.405
DA	0.410	0.966	0.559	0.218

*Significant *p*-value < 0.05.

Discussion

The trabecular bone structure is known as a porous structure which contributes to maximum strength while giving the bone less weight. Understanding the bone marrow flow and trabecular bone structure mechanism can provide insight into bone remodelling process and bone strength. It is vital to identify which architectural features that affect the trabecular strength. Thus, in this study, finite element analysis with FSI approach was used to identify the architecture contribution with the presence of bone marrow when there is physical loading involved.

During physiological activities, the bone will have a deformation due to the mechanical load.[3] The compressive and tensile stress is generated in the trabecular structure which causes the bone marrow within the structure to drift from region of compression to tension. Due to the complex structure of trabecular bone with small rods, plated and pores, there will be shear stress generated on the wall structure. Bone marrow function in activating the bone cells to start the bone remodelling process. Thus, this study analysed shear stress, pressure, and permeability to identify the fluid characteristic through physical activity. Moreover, the trabecular bone architecture and volume fraction play an important role in its mechanical properties. In addition, this study analysed the bone marrow permeability and trabecular stiffness with correlation to the trabecular morphology. Applied physiological gait loading in this present study to assure more reliable and safer prediction of bone marrow behaviour and trabecular stiffness.

In the analysis, it can be seen that the maximum peak von Mises stress range for all ten models are 91 kN/m^2 to 114 kN/m^2. The maximum value was identified in period 0.14s, which is due to the fact that higher contact force occurs at that period of time (Figure 7). Assessing the von Mises stress in the trabecular model was necessary with purpose of providing new insight in prediction of trabecular structure failure and evaluating the fracture risk. The permeability in this study was also in agreement with results from the literature.

The aim of this study is to identify the bone marrow movement behaviour within the trabecular structure sufficient for bone cell growth based on physiological activity.

Table 3. Morphological parameters of trabecular bone sample with Pearson correlation and p-value in relation with fluid characteristics.

	Velocity		Pressure		Shear Stress	
Morphology Parameters	Pearson Correlation	*p*-value	Pearson Correlation	*p*-value	Pearson Correlation	*p*-value
BV/TV	−0.661	0.969	−0.672	0.168	0.001	0.499
BS/TV	0.388	0.449	0.53	0.585	0.411	0.119
SMI	0.710	0.022*	0.825	0.003*	0.029	0.469
Conn. D	−0.049	0.316	0.288	0.815	0.184	0.306
Tb.Th	−0.296	0.395	−0.346	0.209	−0.424	0.111
Tb.Sp	0.607	0.735	0.594	0.754	−0.255	0.239
DA	0.324	0.468	0.074	0.721	0.079	0.414

*Significant *p*-value < 0.05.

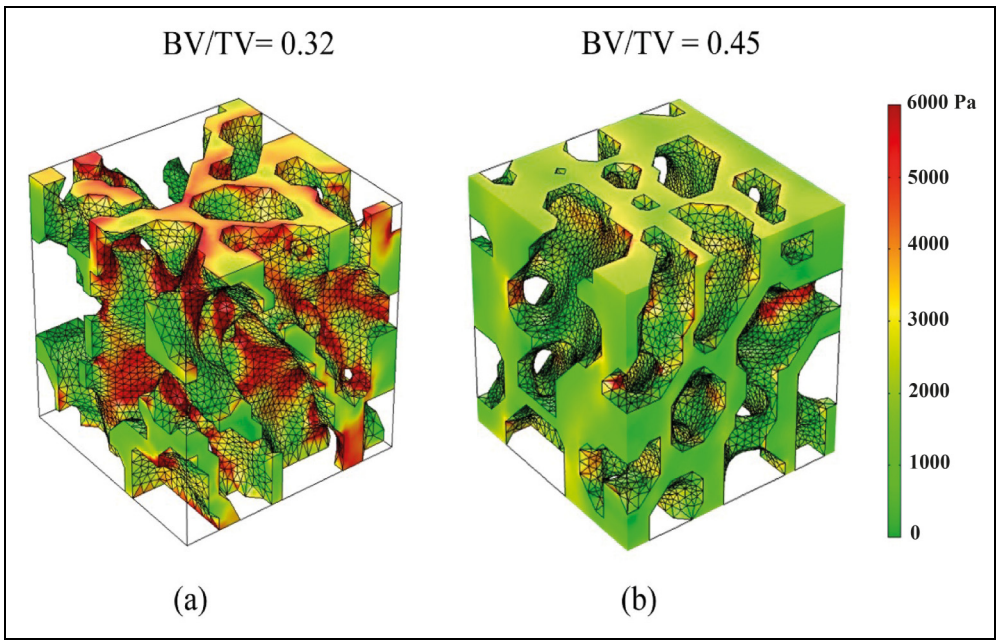

Figure 11. Comparison of von Mises stress on the trabecular bone with different bone fraction (a) BV/TV = 0.32 and (b) BV/TV = 0.45.

Normal walking loading was chosen since it is reported as the most frequent physiological activity.[26] The results show that during normal walking loading, the maximum shear stress occurs is all models are in range 0.05 Pa to 0.27 Pa. Furthermore, Li et al.'[17] Castillo and Jacobs[20] present that the shear stress was needed for the cells to differentiate and proliferate. Moreover, the previous experimental study showed that shear stress in the range of 0.1 Pa to 1 Pa needed to stimulate bone cells in vitro. Thus, a much lower range of shear stress is suggested to simulate the stress on bone cells during normal walking. However, other previously study mention that 0.23 Pa of shear stress is sufficient for regulated bone cells to respond and synthesise bone matrix protein for bone remodelling process.[33] Additionally, there is separate study by Nauman et al.[34] stated that the bone cells stimulation is unaffected by difference shear stress levels.

Walking 10000 step per day has been proposed as daily activity for healthy adults. This recommendation was studied, and it is found that 10000 step per day can improve individual's health and sustainability. For example, previous studies stated higher step count per day could lower the prevalence of depression.[35] In addition, it is observed the Body Mass Index (BMI) of the group with higher step count per day has shown significantly lower compared with another group.[36] Nevertheless, there is no studies indicate on bone health based on daily step count. However, based on the results of this study, it is suggested that higher step count will lead to more shear stress. Thus, can help in improving the bone remodelling process and bone strength.

Moreover, while the trabecular bone deforms according to the physiological load, there would be pressure difference within the structure (Figure 8). Previous study stated bone formation increase with pressure. Welch et al.[37] in their study found that bone marrow pressure increased about 2000 Pa resulted in bone remodelling. Another study on the new bone formation of mouse tibiae, stated in dynamic compression induced a similar range of pressure value.[38] This study results for pressure distribution in normal walking gait loading for all models was in the range of 180 Pa to 4000 Pa. Addition to this study result analysis, it is found that higher bone volume fraction will lead to lower pressure value (Table 3). However, the pressure difference also depends on a variety of factors, including the bone marrow rheology, bone strain and permeability.[39,40]

In addition, the results show that the pressure gradient along the walking gait loading was different at period 0.14s and 0.86 s as in Figure 9. This is where the bone marrow function as hydraulic stiffening effect. Hydraulic stiffening effect refers to the reduction of bone stress during dynamic loading effect by the presence of fluid within the structure.[41] While at period 0.14s is when the maximum compression occurs, the pressure of bone marrow was high at the bottom. This pressure might support a certain amount of applied load which caused the apparent stiffness to the trabecular structure. Similarly, at period of 0.86s, where tensile occur, the pressure was high at the upper region giving the structure extra load barrier which prevents the structure to have high deformation.

This study used BoneJ plugin in the ImageJ software to analyse the morphological data of the trabecular model. In the correlation study, only bone volume fraction (BV/TV) and SMI shows a significant value with the simulation results. Thus, this study correlated the permeability and

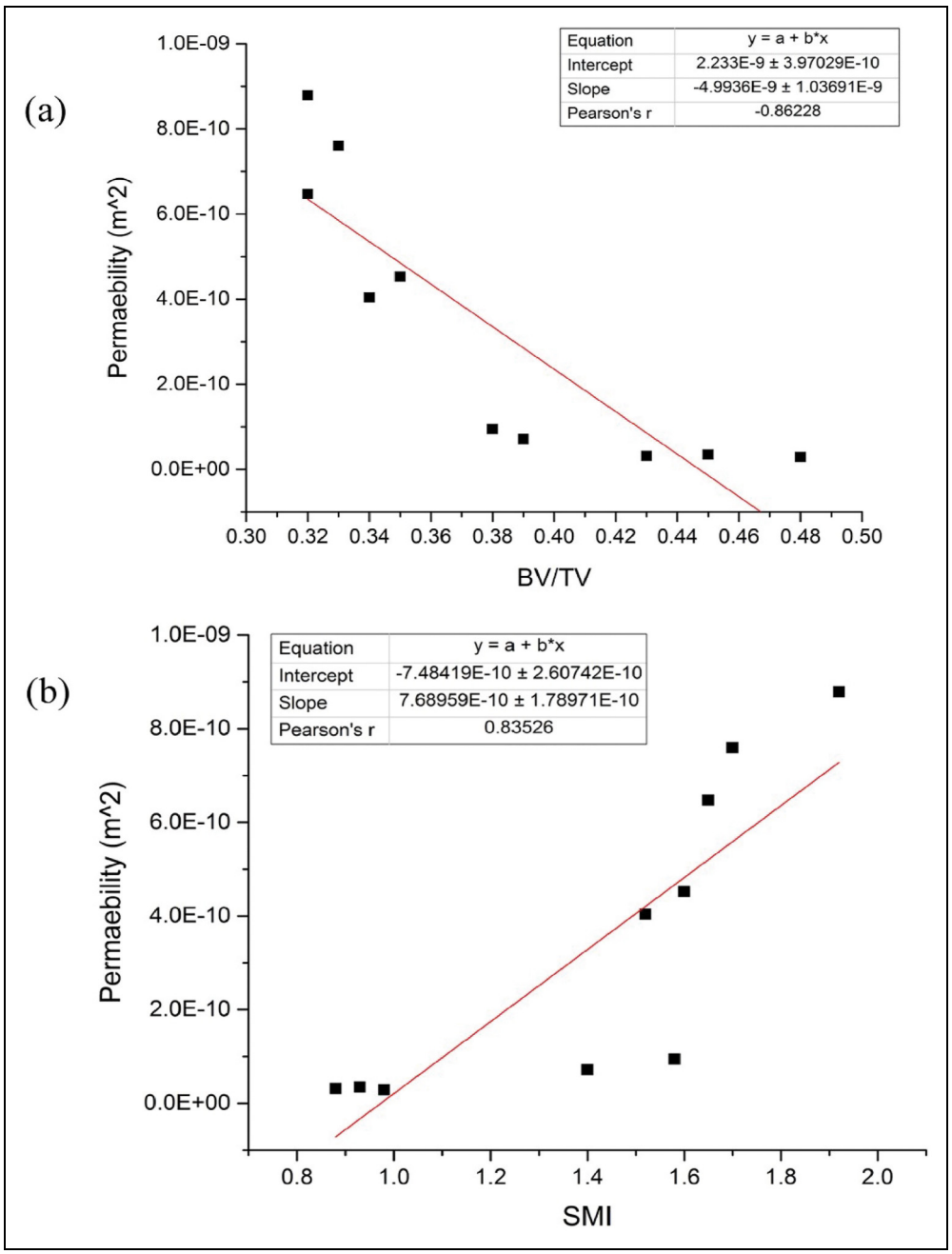

Figure 12. Linear relationship between (a) BV/TV and (b) SMI with permeability.

bone stiffness with these both morphological parameters. From the results, permeability and stiffness show good correlation with the BV/TV. Permeability in trabecular bone was vital since it demonstrated the biological based features of trabecular bone. Still, the simulation results were consistent to those found in the previous literature.[42] Additionally, the trabecular bone mechanical quality was depending on its stiffness, since the stiffness have a strong correlation with the strength.[43]

Hypothetically bone with lower bone volume fraction means porous structure (osteoporotic bone). Thus, as mention by Goldstein et al.[44] and Syahrom et al.,[45] the trabecular bone integrity and bone marrow permeability can be disarrange based on the porosity value. In addition, the results of this study suggests that enhancement of bone remodelling process can be achieved by optimization of BV/TV and permeability value. However, from the results analysis the reduction of BV/TV can cause higher stress on the trabecular structure (Figure 11) and the loss of trabecular structure stiffening effect (Figure 13). Therefore, important to find the optimum bone volume fraction which has a good stiffening value and yet able to deliver sufficient nutrient to bone cells.

Other than bone volume fraction, the SMI also shows high correlation with the stiffness. The SMI is a measurement which determines a porous structure is made of rod or plate-like structure. The value starts from 0 for ideal plate structures to 3 for ideal rod structure.[46]

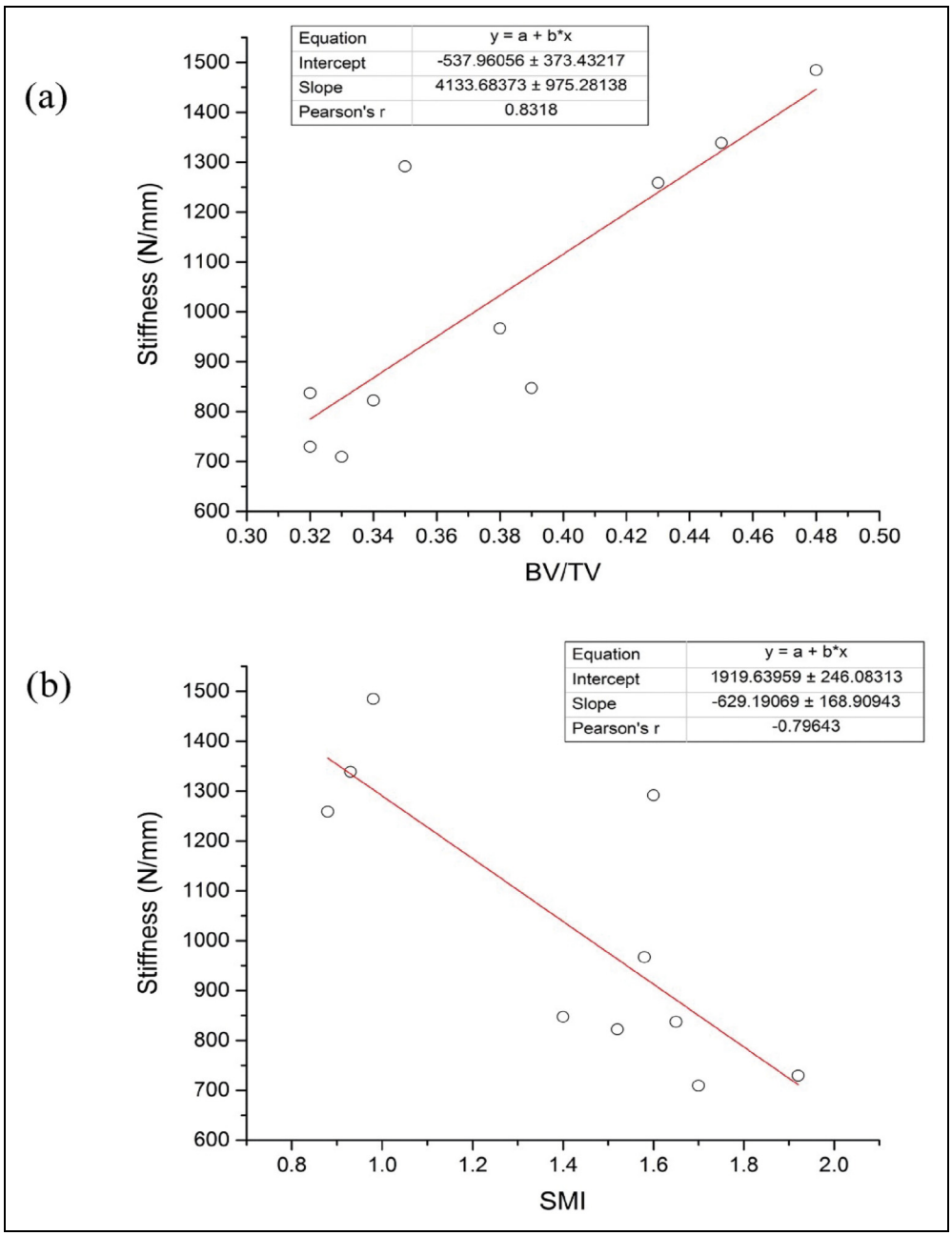

Figure 13. Linear relationship between (a) BV/TV and (b) SMI with stiffness.

Theoretically, the plate-like structure could barricade more fluid flow compared to the rod-like structure. In contrast with the permeability, the stiffness is negatively correlated with the SMI. Moreover, previous study already stated that trabecular plates have more dominant role in mechanical integrity of trabecular bone structure.[47,48] Also, osteoporotic trabecular bone has been found to have an apparent transition of microarchitecture, which is from plate like to rod-like structure.[47] Stein et al.[49] in their study found that the bone stiffness related with trabecular connectivity, trabeculae orientation and trabecular plates. Thus, in correspondence to previous studies, our results suggest that plate-like trabecular structure (lower SMI value) can contribute to higher trabecular stiffness.

There are a few limitations in the interpretation of results that should be considered. This study has employed trabecular samples from anatomic site of bovine femoral bone. As such, the microarchitecture parameters may differ from that of the human bone or other anatomic sites. However, there are a few works done that demonstrate agreement between the architecture as well as mechanical properties of bovine trabecular bone and that of a healthy human.[50,51] Furthermore, the impact of marrow phase on the trabecular structure can be further investigated in terms of its properties such as the variation of constituents and viscosity.

In summary, this study was investigated on the correlation of the morphology parameters onto the mechanical properties of trabecular bone with presence of bone

marrow. The bone volume fraction and SMI were identified as the one that has a higher correlation with the trabecular permeability and stiffness compared with others morphological parameters. Moreover, the bone marrow behaviour through the physiological activity was identified in this study. This study provides insight into understanding how human daily physiological activities contribute to the bone remodelling process and nutrient transport with the bone environment. However, more knowledge in this area was crucial to studying the bone adaption to the bone replacement and in estimating fracture risk.

Conclusion

The overall aim of this study was to assess the importance on the interaction between the bone marrow and trabecular bone structure during mechanical loading by using the FSI approach. Trabecular bone is known as a highly porous structure with a significant volume of bone marrow, a compressive or tensile force on the trabecular bone will result in bone marrow movement with respect to the trabecular bone structure. It is believed that the fluid flow will cause the shear stress to the trabecular structure. The interaction between the fluid and trabecular bone will occur, and this incident might have several effects on the trabecular structure. Moreover, bone remodelling process was occurring due to the shear stress on the bone cell which triggers the process. In addition to shear stress, based on previous study the hydraulic stiffening effect occurs due to the presence of bone marrow within the trabecular bone structure. Therefore, this study proposed the used of FSI approach to model the trabecular bone behaviour and marrow flow characteristic.

The physiological activities in daily human life play a major role than calcium intake in the bone development process.[52] It contributes to mechanical stimuli in bone marrow and trabecular bone strain. Normal walking is one of human major daily activity is chosen in this study as a boundary condition in analysing the trabecular bone behaviour. The bone marrow behaviour was recorded during the normal walking cyclic loading. While the trabecular bone deforms according to the physiological load, the bone marrow within will encounter mechanical stimulation in mechanobiological response.[53,54] The shear stress value along normal walking gait loading was found in a range of 0.05 to 0.27 Pa which is sufficient to regulate cell response minimally.[33] However, due to ageing factor, bone resorption rate will become higher. Thus, higher shear stress was needed in order to have rapid bone remodelling process to encounter the bone resorption rate. Furthermore, this study also provides insight into understanding the related mechanobiological of bone cells and disease in deterioration of nutrient supplied to the bone.

Acknowledgements

This project was sponsored by the Universiti Teknologi Malaysia (UTM) and Universitas Airlangga (Unair) through the Grant scheme (R.J130000.7309.4B535) matching grant scheme. The authors would also like to thank the Research Management Centre, Universiti Teknologi Malaysia, for managing the project.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the Universiti Teknologi Malaysia, (grant number R.J130000.7309.4B535).

ORCID iDs

Andreas Öchsner https://orcid.org/0000-0002-8844-3206
Ardiyansyah Syahrom https://orcid.org/0000-0001-7278-5861

References

1. Saad APM and Syahrom A. Study of dynamic degradation behaviour of porous magnesium under physiological environment of human cancellous bone. *Corros Sci* 2018; 131: 45–56.
2. Yourek G, McCormick SM, Mao JJ, et al. Shear stress induces osteogenic differentiation of human mesenchymal stem cells. *Regen Med* 2010; 5: 713–724.
3. Coughlin TR and Niebur GL. Fluid shear stress in trabecular bone marrow due to low-magnitude high-frequency vibration. *J Biomech* 2012; 45: 2222–2229.
4. Vaughan T, Voisin M, Niebur G, et al. Multiscale modeling of trabecular bone marrow: understanding the micromechanical environment of mesenchymal stem cells during osteoporosis. *J Biomech Eng* 2015; 137: 1–10.
5. You L, Cowin SC, Schaffler MB, et al. A model for strain amplification in the actin cytoskeleton of osteocytes due to fluid drag on pericellular matrix. *J Biomech* 2001; 34: 1375–1386.
6. Adachi T, Kameo Y and Hojo M. Trabecular bone remodelling simulation considering osteocytic response to fluid-induced shear stress. Philosophical transactions of the royal society A: mathematical. *Phys Eng Sci* 2010; 368: 2669–2682.
7. Wittkowske C, Reilly GC, Lacroix D, et al. In vitro bone cell models: impact of fluid shear stress on bone formation. *Front Bioeng Biotechnol* 2016; 4: 87.
8. Birmingham E, Niebur G, McNamara L, et al. An experimental and computational investigation of bone formation in mechanically loaded trabecular bone explants. *Ann Biomed Eng* 2016; 44: 1191–1203.
9. Shen V, Liang X, Birchman R, et al. Short term immobilization-induced cancellous bone loss is limited to regions undergoing high turnover and/or modeling in mature rats. *Bone* 1997; 21: 71–78.
10. Rodriguez N, Herndon D and Klein G. Evidence against a role of immobilization in the bone loss following burns. *Bone* 2011; 2: S190.
11. Frost HM. Wolff's Law and bone's structural adaptations to mechanical usage: an overview for clinicians. *Angle Orthod* 1994; 64: 175–188.

12. Frost HM. Bone "mass" and the "mechanostat": a proposal. *Anat Rec* 1987; 219: 1–9.
13. Burr DB, Milgrom C, Fyhrie D, et al. In vivo measurement of human tibial strains during vigorous activity. *Bone* 1996; 18: 405–410.
14. Fritton SP, McLeod KJ and Rubin CT. Quantifying the strain history of bone: spatial uniformity and self-similarity of low-magnitude strains. *J Biomech* 2000; 33: 317–325.
15. Gurkan UA and Akkus O. The mechanical environment of bone marrow: a review. *Ann Biomed Eng* 2008; 36: 1978–1991.
16. McAllister T and Frangos J. Steady and transient fluid shear stress stimulate NO release in osteoblasts through distinct biochemical pathways. *J Bone Miner Res* 1999; 14: 930–936.
17. Li YJ, Batra NN, You L, et al. Oscillatory fluid flow affects human marrow stromal cell proliferation and differentiation. *J Orthop Res* 2004; 22: 1283–1289.
18. Knight MN and Hankenson KD. Mesenchymal stem cells in bone regeneration. *Adv Wound Care* 2013; 2: 306–316.
19. Shao J, Zhang W and Yang T. Using mesenchymal stem cells as a therapy for bone regeneration and repairing. *Biol Res* 2015; 48: 62.
20. Castillo AB and Jacobs CR. Mesenchymal stem cell mechanobiology. *Curr Osteoporos Rep* 2010; 8: 98–104.
21. Klein–Nulend J, Van Der Plas A, Semeins CM, et al. Sensitivity of osteocytes to biomechanical stress in vitro. *FASEB J* 1995; 9: 441–445.
22. Case N, Sen B, Thomas J, et al. Steady and oscillatory fluid flows produce a similar osteogenic phenotype. *Calcif Tissue Int* 2011; 88: 189–197.
23. Bakker AD, Joldersma M, Klein-Nulend J, et al. Interactive effects of PTH and mechanical stress on nitric oxide and PGE2 production by primary mouse osteoblastic cells. *Am J Phys-Endocrinol Metab* 2003; 285: E608–EE13.
24. Arnsdorf EJ, Tummala P, Kwon RY, et al. Mechanically induced osteogenic differentiation–the role of RhoA, ROCKII and cytoskeletal dynamics. *J Cell Sci* 2009; 122: 546–553.
25. Yeatts AB and Fisher JP. Bone tissue engineering bioreactors: dynamic culture and the influence of shear stress. *Bone* 2011; 48: 171–181.
26. Bergmann G, Deuretzbacher G, Heller M, et al. Hip contact forces and gait patterns from routine activities. *J Biomech* 2001; 34: 859–871.
27. Fatihhi S, Harun M, Kadir MRA, et al. Uniaxial and multiaxial fatigue life prediction of the trabecular bone based on physiological loading: a comparative study. *Ann Biomed Eng* 2015; 43: 2487–2502.
28. Homminga J, Mccreadie BR, Weinans H, et al. The dependence of the elastic properties of osteoporotic cancellous bone on volume fraction and fabric. *J Biomech* 2003; 36: 1461–1467.
29. Sylvester AD and Kramer PA. Young's modulus and load complexity: modeling their effects on proximal femur strain. *Anat Rec* 2018; 301: 1189–1202.
30. Bayraktar HH, Gupta A, Kwon RY, et al. The modified super-ellipsoid yield criterion for human trabecular bone. *J Biomech Eng* 2004; 126: 677–684.
31. Bryant J, David T, Gaskell P, et al. Rheology of bovine bone marrow. Proceedings of the institution of mechanical engineers. *Part H: J Eng Med* 1989; 203: 71–75.
32. Haskill JS, McNeill TA and Moore MAS. Density distribution analysis of In vivo and In vitro colony forming cells in bone marrow. *J Cell Physiol* 1970; 75: 167–179.
33. Kreke MR, Sharp LA, Woo Lee Y, et al. Effect of intermittent shear stress on mechanotransductive signaling and osteoblastic differentiation of bone marrow stromal cells. *Tissue Eng, Part A* 2008; 14: 529–537.
34. Nauman E, Satcher R, Keaveny T, et al. Osteoblasts respond to pulsatile fluid flow with short-term increases in PGE2 but no change in mineralization. *J Appl Physiol* 2001; 90: 1849–1854.
35. McKercher CM, Schmidt MD, Sanderson KA, et al. Physical activity and depression in young adults. *Am J Prev Med* 2009; 36: 161–164.
36. Krumm EM, Dessieux OL, Andrews P, et al. The relationship between daily steps and body composition in postmenopausal women. *J Womens Health (Larchmt)* 2006; 15: 202–210.
37. Welch R, Johnston 2nd C, Waldron M, et al. Bone changes associated with intraosseous hypertension in the caprine tibia. *JBJS* 1993; 75: 53–60.
38. Hu M, Cheng J and Qin Y-X. Dynamic hydraulic flow stimulation on mitigation of trabecular bone loss in a rat functional disuse model. *Bone* 2012; 51: 819–825.
39. Teo J, Si-Hoe K, Keh J, et al. Correlation of cancellous bone microarchitectural parameters from microCT to CT number and bone mechanical properties. *Mater Sci Eng C* 2007; 27: 333–339.
40. Baroud G, Falk R, Crookshank M, et al. Experimental and theoretical investigation of directional permeability of human vertebral cancellous bone for cement infiltration. *J Biomech* 2004; 37: 189–196.
41. Liebschner MA and Keller TS. Hydraulic strengthening affects the stiffness and strength of cortical bone. *Ann Biomed Eng* 2005; 33: 26–38.
42. Kohles SS and Roberts JB. Linear poroelastic cancellous bone anisotropy: trabecular solid elastic and fluid transport properties. *J Biomech Eng* 2002; 124: 521–526.
43. Goulet RW, Goldstein SA, Ciarelli MJ, et al. The relationship between the structural and orthogonal compressive properties of trabecular bone. *Journal of Biomechanics* 1994; 27(4): 375–389.
44. Goldstein AS, Juarez TM, Helmke CD, et al. Effect of convection on osteoblastic cell growth and function in biodegradable polymer foam scaffolds. *Biomaterials* 2001; 22: 1279–1288.
45. Syahrom A, Kadir MRA, Abdullah J, et al. Permeability studies of artificial and natural cancellous bone structures. *Med Eng Phys* 2013; 35: 792–799.
46. Hildebrand T and Rüegsegger P. Quantification of bone microarchitecture with the structure model index. *Comput Methods Biomech Bio Med Eng* 1997; 1: 15–23.
47. Wang J, Zhou B, Liu XS, et al. Trabecular plates and rods determine elastic modulus and yield strength of human trabecular bone. *Bone* 2015; 72: 71–80.
48. Wang J, Zhou B, Parkinson I, et al. Trabecular plate loss and deteriorating elastic modulus of femoral trabecular bone in intertrochanteric hip fractures. *Bone Res* 2013; 1: 346–354.
49. Stein EM, Kepley A, Walker M, et al. Skeletal structure in postmenopausal women with osteopenia and fractures is characterized by abnormal trabecular plates and cortical thinning. *J Bone Miner Res* 2014; 29: 1101–1109.
50. Keaveny TM, Wachtel EF, Ford CM, et al. Differences between the tensile and compressive strengths of bovine

tibial trabecular bone depend on modulus. *J Biomech* 1994; 27: 1137–1146.
51. Morgan EF, Yeh OC, Chang WC, et al. Nonlinear behavior of trabecular bone at small strains. *J Biomech Eng* 2001; 123: 1–9.
52. Anderson JJ. The important role of physical activity in skeletal development: how exercise may counter low calcium intake. *Am J Clin Nutr* 2000; 71: 1384–1386.
53. Metzger TA, Schwaner SA, LaNeve AJ, et al. Pressure and shear stress in trabecular bone marrow during whole bone loading. *J Biomech* 2015; 48: 3035–3043.
54. Birmingham E, Grogan J, Niebur G, et al. Computational modelling of the mechanics of trabecular bone and marrow using fluid structure interaction techniques. *Ann Biomed Eng* 2013; 41: 814–826.