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EDITED BY
Lia Rimondini,
University of Eastern Piedmont, Italy

REVIEWED BY
Ksenia Menshikh,
Università del Piemonte Orientale, Italy
Francesco Baino,
Politecnico di Torino, Italy

*CORRESPONDENCE
Meng Wang,
wangmeng@hrbmu.edu.cn

†These authors have contributed equally to this work

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Biomaterial-based strategy for bone tumor therapy and bone defect regeneration: An innovative application option

Yue Zhang[1], Yunjiao Wu[1], Xinyi Qiao[1], Tie Lin[2†], Yicun Wang[3†] and Meng Wang[1*]

[1]Department of Medical Oncology, Harbin Medical University Cancer Hospital, Harbin, China, [2]Department of Surgery, The First Affiliated Hospital of Harbin Medical University, Harbin, China, [3]Jilin Provincial Key Laboratory on Molecular and Chemical Genetic, The Second Hospital of Jilin University, Changchun, China

Bone tumors are deadly and incurable diseases that invade large areas of bone, resulting in bone defects. Traditional therapies combining surgery, chemotherapy, and radiation have reached their limit of efficacy, motivating efforts to develop new therapeutic methods. Fortunately, the development of biomaterials provides innovative options for bone tumor treatment. Suitable biomaterials are capable of simultaneously providing tumor therapy and promoting bone regeneration. This review summarizes recent progress in the effort to achieve new strategies for bone tumor treatment using biomaterials, focusing on the innovative scaffold design. It also discusses the development of nanocarrier-based drug delivery systems and hyperthermia therapy for bone tumor treatment. In the future, biomaterial-based strategies are likely to become the most effective and reliable options for treating bone tumors, and they have the potential to greatly improve the prognosis and quality of life for patients.

KEYWORDS

bone tumor, biomaterial, bone regeneration, drug delivery, hyperthermia therapy

Introduction

Epidemiology and clinical background of bone tumor

Bone tumors can be broadly divided into primary bone tumors (sarcomas) and secondary bone tumors (metastases). Primary bone tumors are uncommon (comprising approximately only 0.2% of malignant tumors) in all age groups (Jiang et al., 2020). These tumors are heterogeneous, including osteosarcomas, chondrosarcomas, and Ewing sarcomas, which are mostly diagnosed in childhood and adolescence (Ambrosio et al., 2021). Approximately 30% of patients with primary bone tumors die within 5 years due to poor response to treatment. Metastatic bone tumors are frequent complications of many cancers at a later stage, with a high incidence in breast and prostate cancer in particular. Bone metastasis has a 5-year survival rate of only 10% as a result of poor prognosis (Gonzalez Diaz et al., 2019). Due to their high degree

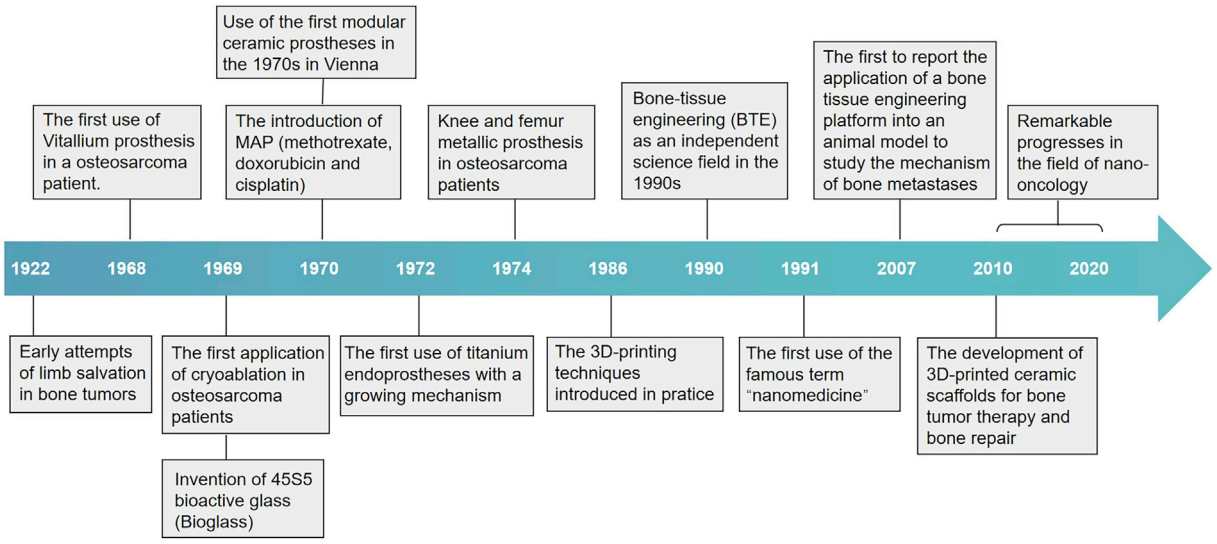

FIGURE 1
Timeline of major milestones in the development of materials for bone repair and osteosarcoma treatment. The development of materials for bone repair began in the 1920s with the use of calcium phosphates and metal substitutes to replace lost bone at defect sites. Other forms of materials have been introduced throughout the subsequent years, such as bioglass and polymer materials, and bone-tissue engineering eventually arose as an independent field. The advent of 3D printing fabrication opened the path to designing bioactive scaffolds, which are the focus in the field of bone-tissue engineering. Furthermore, bone-tissue engineering has witnessed some emerging fields, including biomaterials science, nanotechnology, and their convergence with 3D printing, in the last few years. These fields have been dynamically evolving due to urgent needs from clinical applications.

of malignancy and complexity, strong invasiveness, and considerable mortality, bone tumors bring great suffering to patients.

Treatment strategies for bone tumor

In the clinic, conventional therapies for bone tumors mainly include surgical interventions, chemotherapy, and radiotherapy. Unfortunately, surgical resection often fails to completely eradicate micrometastases, which is likely to result in postoperative recurrence and metastasis (Chen and Yao, 2022). In some cases, bone defects caused by surgery are the main cause of physical disability. Sometimes, attempts are made to eliminate tumors exclusively with chemotherapy and radiotherapy. However, drug resistance and strong side effects can appear during chemotherapy. Additionally, some bone tumors such as osteosarcoma are not sensitive to radiotherapy and are inclined to chemotherapy resistance (Miwa et al., 2021). Considering the challenges in bone tumor treatment and the clinical need for new approaches, in the last few years, researchers have focused on creating innovative biomaterials with the ability to elicit specific cell behaviors that are needed for both tumor therapy and bone tissue regeneration (Guerrieri et al., 2020).

Emergence and development of materials for bone repair

In the first attempt of its kind, an American surgeon tried to implant calcium phosphates to repair damaged bone in the early 20th century (Dorozhkin, 2013). Implants designed to repair bone defects have since evolved, with some offering different levels of structural support and some stimulating bone regeneration using osteoinductive materials (Giannoudis et al., 2005). Various materials have been developed over the years, and bone-tissue engineering eventually arose as an independent scientific field in the 1990s (Koons et al., 2020). Bone-tissue engineering has witnessed the rise of some emerging fields, including biomaterial science, developmental and molecular science, and nanotechnology. In the past decade, research in these fields has inspired innovation in new biomaterials, scaffold design, fabrication techniques, and applications. Herein, we review the history of materials for bone repair and provide more details on osteosarcoma treatment, as this field has been dynamically developing due to urgent clinical needs. The timeline of major milestones in the progress of material development for bone repair and osteosarcoma treatment is illustrated in Figure 1.

TABLE 1 Examples of biomaterial scaffolds used in bone tumor therapy and bone regeneration.

Biomaterial	*In vitro* model	*In vivo* model	Effect(s)	Type	References
Fe-$CaSiO_3$ composite scaffolds	Human osteosarcoma cells (Saos-2)	Femoral defect models in rabbits	Synergistic photothermal and ROS tumor therapy; the bioactive ions improve osteogenic activity	Photothermal therapy	Ma et al. (2018)
Nb_2C MXer-functionalized scaffolds	Human osteosarcoma cells (Saos-2)	Cranial defect model in SD rats	NIR effect on ablating tumor cells and the ability to promote mineralization	Photothermal therapy	Yin et al. (2021)
PLGA/Mg LT-RP 3D-printed scaffolds	Human osteosarcoma cells (Saos-2)	Distal femur defect rat model	Photothermal effect to suppress tumor recurrence and the healing process by accelerating bone remodeling	Photothermal therapy	Long et al. (2021)
Cu-MSN-Tcp scaffolds via spin coating	Human osteosarcoma cells (MG-63)		Bone tumor cell apoptosis and necrosis by hyperthermia and gene expression of osteogenic markers	Photothermal therapy	Ma et al. (2020)
Tricalcium phosphate scaffolds co-loaded with genistein, daidzein and glycitein	Human osteosarcoma cells (MG-63)	Distal femur defect rat model	Localized bone tumor cell suppression and bone cell proliferation	Drug delivery system	Sarkar and Bose, (2020)
Coloaded Fe_3O_4 and CaO_2 nanoparticle scaffolds	MNNG/HOS osteosarcoma tumor cells	Cranial defects in SD rats	Useful photothermal therapy for bone tumor	Photothermal therapy	Dong et al. (2019)
Hydrogenated black TiO_2 coating with biomimetic structures deposited on a titanium implant	Human osteosarcoma cells (Saos-2)		Photothermal ablation to stimulate bone tumor cell necrosis and adhesion; proliferation and osteogenic differentiation of rBMSCs	Photothermal therapy	Zhang et al. (2019)
Hydrogel containing cisplatin (DPP) and polydopamine-decorated nano-hydroxyapatite	Mouse breast cancer (4T1) cells and human normal breast (MCF-10A) cells	Tumor model in BALB/c mice	Synergistic local hyperthermia and drugs to ablate tumors promptly; enhanced bone repair	Photothermal therapy	Luo Y. et al. (2019)
A composite scaffold of nano-hydroxyapatite (nHA) and reduced graphene oxide (rGO)	Human osteosarcoma cells (MG-63)	Rat calvaria defect model	Photothermal effect on killing tumor cells and enhancing bone regeneration in rBMSCs	Photothermal therapy	Li L. et al. (2018)
Distributing Fe_3O_4 nanoparticles inside PMMA cement scaffolds		Tibial plateau bone tumor in rabbits	Superior bone tumor ablation upon exposure to an AMF and mechanical support for bone repair	Magnetothermal therapy	Yu et al. (2019)
Bioactive chitosan (CS) matrix incorporating Fe_3O_4 nanoparticles and $GdPO_4$ nanorods	MC3T3-E1, RAW264.7 and MDA-MB-231 (breast cancer bone metastasis tumor cells)	Calvarial-defect models in rats and implantation in nude mice	Photothermal ablation to eradicate postoperative residual tumors; nanorod to promote angiogenesis; and osteogenesis for bone defect healing	Photothermal therapy	Zhao et al. (2020)
$SrFe_{12}O_{19}$-modified bioglass (BG)/chitosan (CS) scaffolds	Human osteosarcoma cells (MG-63)	Calvarial-defect models in rats	Magnetothermal therapy in MG-63 bone tumors; scaffolds to enhance bone regeneration	Photothermal therapy	Lu et al. (2018)
$CuFeSe_2$-functionalized BG scaffolds	Human osteosarcoma cells (Saos-2)	Femoral defect models in rabbits	Metal elements in BG to endow BG with both photothermal effect and bone regeneration ability	Photothermal therapy	Dang et al. (2018)

ROS, reactive oxygen species; Nb_2C, 2D niobium carbide; SD, Sprague–Dawle; NIR, near-infrared; PLGA, poly(lactide-co-glycolide); LT-PR, low temperature rapid prototyping; 3D, three-dimension; MSN, mesoporous silica nanosphere; Tcp, tricalcium phosphate; rBMSCs, rat bone marrow stem cells; PMMA, polymethylmethacrylate; AMF, alternating magnetic field.

A new strategy for bone tumor therapy and bone regeneration

The two main challenges in bone tumor therapy are eliminating tumor cells and facilitating bone regeneration (Ma et al., 2018; Liao et al., 2021). Some new therapies have shown strong potential, particularly the biomaterial-based strategy (including targeted drug delivery and hyperthermia therapy), which has demonstrated high anticancer effects (Tan et al., 2021). More importantly, biomaterial scaffolds can provide an ideal *in vivo* environment for cells to grow, proliferate, and differentiate, and they can also leverage the synergistic effect of bioactive molecules for bone tissue repair (Brunello et al., 2020; Tan et al., 2021). Thus, the biomaterial-based strategy is an innovative option that is capable of simultaneously achieving bone tumor therapy and promoting bone regeneration.

In this review, we summarize the recent progress in the development of biomaterials for bone tumor therapy and bone defect regeneration. We describe biomaterial scaffolds created for simultaneous bone tumor therapy and bone regeneration,

focusing on innovative scaffold design. Finally, we also discuss nanocarrier-based drug delivery systems and hyperthermia therapy for bone tumor treatment.

Role of scaffolds

When treating bone defects caused by tumor resection, the design of biomaterials must simultaneously meet the requirements of bone repair and tumor suppression. Therefore, biomaterial selection and structural design are critical (Du et al., 2019). The purpose of a biomaterial scaffold is not to simply replace the missing bone tissue but also to create a biomimetic microenvironment for the growth of cells and tissues by mimicking the natural extracellular matrix. The scaffold must inherit the biomaterial's advantageous properties, such as excellent biocompatibility, adequate mechanical strength, biodegradation, and cell adhesion and transportation (Tevlin et al., 2014).

Types of scaffolds

Biomaterials used in scaffolds can be divided into polymers, bioceramics, carbon containing materials, metals, and hydrogels (Marques et al., 2014). Table 1 shows bioactive scaffolds fabricated for bone tumor treatment and bone regeneration.

Polymers

Polymeric materials have strong potential for application in bone tumor therapy due to their good biocompatibility and design flexibility. According to their origin, polymers can be simply classified into two groups, namely natural polymers and synthetic polymers (Filippi et al., 2020).

Natural polymers used for bone tissue regeneration mainly include collagen, gelatin, chitosan, and alginate (Marques et al., 2014; Zhao et al., 2020). They are similar to the components in the native extracellular matrix, ensuring superior biocompatibility and minute immunogenicity. One potential advantage of natural polymers is that they often contain functional molecules, which is advantageous for cellular adhesion (Bose et al., 2012). However, natural polymers also face many disadvantages. In some cases, pathogenic impurities may exist, which can trigger immunogenic reactions. Other disadvantages include low mechanical strength, poor elastic properties, and less control over degradability, which could limit their use in load-bearing applications (Peric Kacarevic et al., 2020).

Synthetic polymers such as polymethylmethacrylate (PMMA) and poly (lactic-coglycolic acid) (PLGA) have been investigated for bone tumor applications (Yu et al., 2019; Long et al., 2021). Unlike natural polymers, synthetic polymers can be fabricated to meet desired mechanical characteristics and geometric properties. However, poor biocompatibility and unsatisfactory hydrophilicity limit clinical applications of synthetic polymers. Furthermore, synthetic polymers produce undesirable degradation products and create a local acidic environment, which can have cytotoxic effects and cause inflammatory responses (Bharadwaz and Jayasuriya, 2020).

Bioceramics

Calcium phosphate ceramics, including hydroxyapatite (HA), β-tricalcium phosphate, and bioactive glass (BG), are commonly used for orthopedic applications, as calcium phosphate is abundant in native human bone (Luo S. et al., 2019; Dang et al., 2018; Lu et al., 2018; H. Ma et al., 2020). Hydroxyapatite is present in natural bone as an inorganic component of bone matrix. It has excellent biocompatibility and osteoinduction properties, so it has been widely used in bone defect repair materials and has also been considered as a promising carrier for drug delivery to sites of bone disease (Marques et al., 2014; Tang et al., 2021). Hydroxyapatite could allow strong integration with host tissue, further promoting new bone formation *in vivo* and selectively and efficiently killing tumor cells *in vitro* to achieve the purpose of bone tumor therapy (Luo Y. et al., 2019). The design of bioceramics not only greatly expands bone tumor therapeutic strategies but also represents a new direction for bioceramics science. However, the drawback of brittleness could limit the utility of bioceramics in load-bearing support. Additionally, it is difficult to tune the resorption rate of bioceramics, resulting in a decline of mechanical properties (Turnbull et al., 2018).

Metals

Generally, an ideal metallic material possesses excellent biocompatibility and high mechanical performance, and it releases non-toxic ions. As typical representatives, magnesium (Mg), titanium, and their alloys are suitable for clinical applications (Huang et al., 2020). However, poor corrosion resistance could induce tissue reactions and raise the risk of loosening. The higher elastic modulus of metals relative to natural bone can also result in bone resorption and therapeutic failure. In addition, poor biodegradability may lead to further impairment of tissue ingrowth (Turnbull et al., 2018). However, surface modification has been applied to improve bioactivity in traditional biomaterials. It enhances metallic corrosion resistance and promotes osteoblast attachment through coating, showing superior osteogenesis and integration ability (Zhang et al., 2019).

Carbon and other nanoparticles

It is well known that scaffolds have been significantly improved using nanobiological materials (Quadros et al.,

TABLE 2 Drug delivery systems developed for the treatment of osteosarcoma.

Nanoparticle type	Drug carrier	Chemotherapeutic drugs	References
Polymeric nanoparticles	Coupling of Methotrexate with PGA nanoparticles	Methotrexate	Suksiriworapong et al. (2018)
Polymeric nanoparticles	Keratin nanoparticles functionalized by Chlorin-e6	Paclitaxel	Martella et al. (2018)
Polymeric nanoparticles	PLGA nanoparticles	Salinomycin	Irmak et al. (2020)
Polymeric nanoparticles	Poly (ester amide)	Apatinib	Li et al. (2020b)
Polymeric nanoparticles	Poloxamers modified with trimethyl chitosan	Methotrexate	Li et al. (2017)
Polymeric micelles	HA-octadecanoic acid (contains alendronate)	Curcumin	Xi et al. (2019)
Polymeric micelles	Bone-targeting micelles (contains D-aspartic acid octapeptide)	Doxorubicin	Low et al. (2014)
Polymeric micelles	Micelles with RGD-modified PEG-block-poly (trimethylene carbonate) copolymer	Doxorubicin	Fang et al. (2017)
Polymeric nanogels	HA-based nanogels	Cisplatin and Doxorubicin	Zhang et al. (2018)
Metallic nanoparticles	Fe_3O_4-based nanoparticles	Gemcitabine	Popescu et al. (2017)
Mesoporous silica nanoparticles	PEI-modified and iron oxide-loaded mesoporous silica nanoparticles	Doxorubicin	Hartono et al. (2014)
Carbon nanomaterials	(TRA/GO nano-complexes)	Trastuzumab	Li D. et al. (2018)
Calcium phosphates nanoparticles	Bisphosphonate modified HANPs	JQ1	Wu et al. (2017)
Liposomes	COS modified liposomes	Doxorubicin	Yin et al. (2017)
Liposomes	PEGylated liposomes	Gemcitabine and Clofazimine	Caliskan et al. (2019)
Liposomes	PEGylated liposomes coated with gold nanoshells	Betulinic acid	Liu et al. (2017)
Liposomes	Liposomes modified with alendronic acid and LMWH	Doxorubicin	Wu et al. (2020)

PGA, poly glycerol adipate; PLGA, poly lactideco-glycolic acid; HA, hyaluronic acid; RGD, arginine-glycine-aspartic peptide acid; PEI, polyethyleneimine; HANPs, hydroxyapatite nanoparticles; TRA, trastuzumab; GO, graphene oxide; JQ1, a small-molecule bromodomain inhibitor; COS, chitooligosaccharides; PEG, polyethylene glycol; LMWH, low molecular weight heparin.

2021). Nanomaterials, including polymeric nanoparticles, carbon-based nanomaterials, and metallic nanoparticles, have been designed to permit local drug delivery in bone tumor therapies. They also have excellent photothermal conversion ability and high adsorption ability, so they could serve as photothermal agents (Badila et al., 2021).

Carbon-based materials are potentially useful nanomaterials for bone tumor treatment. Most studied carbon materials for therapeutics are graphene, graphene oxide (GO), and reduced graphene oxide (rGO) (Li D. et al., 2018; Yin et al., 2021). Both GO and rGO are generated through graphene conversion (Geetha Bai et al., 2019). Graphene has exceptional mechanical properties, favorable osteoinductivity, and a large surface area. It can provide active sites that support cell differentiation, growth, and proliferation. However, the cytotoxicity of graphene and its derivatives has always been problematic (Fang et al., 2022).

With the development of biomaterial science, inorganic nanoparticles have also made their way into therapeutics through the use of nanotechnology (Fang et al., 2022). Metal nanoparticles such as Fe and Cu, which have been incorporated into scaffolds, have shown potential in promoting the proliferation and differentiation of mesenchymal stem cells (MSCs) in animal models (Dang et al., 2018; Lu et al., 2018; Ma et al., 2018).

Hydrogels

Hydrogels possess good biocompatibility, biodegradability, injectability, and the ability to load growth factors, meaning they have the potential to repair bone defects (Fang et al., 2022). Some new injectable hydrogels prepared through chemical reactions have been applied to bone tumor treatment. They not only effectively ablate bone tumor cells *via* photothermal effects but also support the attachment, proliferation, and osteogenic differentiation of bone MSCs. In addition, they can be used for more accurate targeted delivery of anticancer drugs and fixation of bone defect tissue (Yu and Ding, 2008; Luo S. et al., 2019). Although hydrogels are still in development, the prospect of multifunctional hydrogel-based materials has been strongly demonstrated in anticancer treatment and bone repair.

Enhancing regenerative capacity of biomaterials: Seed cells and growth factors

To engineer the ideal biomaterial scaffold, osteoinductive bioactive components, such as growth factors and progenitor

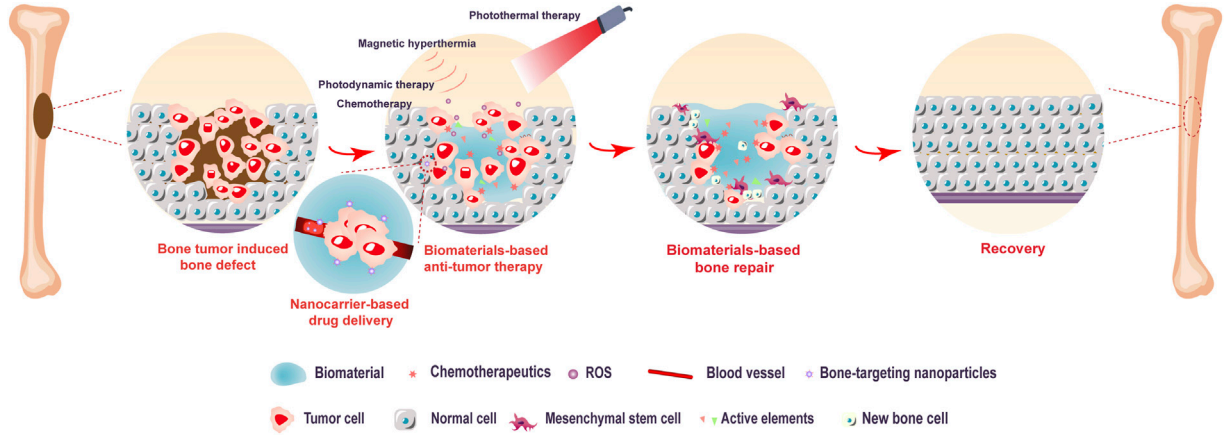

FIGURE 2
Biomaterial-based bone tumor and bone repair scheme. The biomaterial-based strategy (including targeted chemotherapy, photothermal therapy, photodynamic therapy, and magnetic hyperthermia) demonstrates a high anticancer effect in the early stage. Additionally, biomaterials with great osteoinductivity support the attachment, proliferation, and differentiation of mesenchymal stem cells in bone tissue repair.

cells, should be successfully recruited for bone regeneration (Qi et al., 2021). The essential stem cell sources provide higher proliferative ability and allow the differentiation of various cell types from a single cell (Vats et al., 2002). MSCs, endothelial progenitor cells (EPCs), and induced pluripotent stem cells (iPSCs) are included in bone progenitor cells. MSCs are currently more suitable for tissue repair since they can differentiate into bone and connective tissues (Vats et al., 2002). The incorporation of growth factors into biomaterial scaffolds can promote cell growth and differentiation for the normal healing response. Growth factors for improving osteogenesis and angiogenesis include vascular endothelial growth factors (VEGF), fibroblast growth factors (FGFs), and bone morphogenic proteins (BMPs) (Brunello et al., 2020; Qi et al., 2021).

Fabrication of Scaffolds-3D printing technology

The development and application of 3D printing technology represents a huge opportunity for bone-tissue engineering. Over the years, this technology has quickly evolved into advanced methods suitable for the fabrication of novel, geometrically intricate, biomimetic biomaterial scaffolds (Nikolova and Chavali, 2019). Moreover, 3D printing technology can be used to design and manufacture living tissue-like structures with properties similar to those of natural bone tissue (Parisi et al., 2018). Additionally, computer-assisted design technologies can be used to generate 3D models that fully resemble native tissue to better mimic cellular interactions and processes (Vats et al., 2002; Koons et al., 2020). Overall, 3D printing is regarded as a revolutionary and powerful tool that has been successfully employed in medicine, especially in the field of tissue engineering. However, it still faces great challenges, and solving these challenges will require multidisciplinary collaboration on the creation of advanced techniques for analysis and quantification.

Nanocarrier-based drug delivery systems and hyperthermia therapy

As one of the widely investigated applications for nanotechnology, nanocarrier-based drug delivery systems offer promise for the treatment of cancers (Bae et al., 2011). Nanomaterials can be used as carriers to encapsulate chemotherapeutic agents to prolong drug circulation time and protect them from rapid clearance (Muntimadugu et al., 2017). Targeting the delivery of drugs to the bone could achieve a high local concentration, enhance therapeutic efficiency, and reduce systemic toxicity (Bae et al., 2011; Lungu et al., 2019). The successful exploration of drug delivery systems will provide new methods for ideal bone tumor therapy, which encourages the development of targeted therapies. Nanocarriers developed for bone tumor mainly include liposomes, polymeric nanoparticles, metallic nanoparticles, carbon-based nanomaterials, and calcium phosphate carriers (Wang et al., 2020). Table 2 summarizes the application of antineoplastic drugs and nanocarriers in osteosarcoma drug delivery systems.

Studies on hyperthermia therapy, such as biomaterials with good photothermal and magnetothermal properties, have demonstrated encouraging outcomes in bone tumor treatment. Photothermal therapy (PTT) employs near-infrared

(NIR) laser photoabsorbers to convert light energy into heat energy to ablate cancer cells (Zou et al., 2016; de Oliveira et al., 2021). Photothermal agents could be used as NIR absorbents and enhancers to increase the efficiency of localized light-based heating (Li et al., 2020a). To date, various types of photothermal agents using biomaterials, such as metal nanomaterials, carbon-based nanoparticles, and biomaterial scaffolds, have been designed and developed for bone tumor treatment (Zou et al., 2016). Photodynamic therapy (PDT) can also selectively induce the death of tumor cells, which is based on the localized generation of oxidative stress, preserving normal tissues (Sibata et al., 2000). It has been proved that giant cell tumors, chondrosarcoma, and osteosarcoma are susceptible to *in vitro* PDT (Hourigan et al., 1993). Magnetic hyperthermia (MHT) is a non-invasive method for bone tumor ablation, and it is based on heat generation by magnetic materials (Sedighi et al., 2021). MHT could achieve localized tumor heating and induces the apoptosis/necrosis of cells by the transformation of electromagnetic energy under an alternating magnetic field (Fatima et al., 2021).

Conclusion and prospects

With the development of material science, biomaterials have attracted increasing attention due to their specific biological properties, excellent tumor specificity, and high drug-loading capacity. One of the major advantages of biomaterials is how precisely they can be controlled with specific structures according to individual defect conditions. Biomaterial scaffolds largely mimic native tissue, with excellent biosafety and minimal biological immune reactions due to the combination of biomaterials and bioactive components, allowing them to be used safely in patients. In recent decades, researchers have attempted to design functional biomaterials for simultaneously killing bone tumor cells and repairing bone defects induced by surgical resection. In addition, multifunctional biomaterial designs enabling bone regeneration, chemotherapy drug delivery, and the anticancer effects of hyperthermia therapy have been constructed. Thus, supplementary or alternative methods based on biomaterials are expected to become integrated bone tumor therapy strategies (Figure 2).

Although many studies have shown that hyperthermia could effectively result in irreversible cell death and tumor destruction by generating high temperatures, it is difficult to avoid damage to normal tissue and other side effects, such as local immune-inflammatory response. Recently, more efficient drug delivery systems incorporating bioactive substances (antibiotics or antineoplastic drugs) have been designed through biomaterial modification, allowing drugs to be released *in situ* (Andronescu et al., 2013). However, the precise control of drug distribution in space and time is a challenge still faced by drug delivery systems, so further studies are needed. Last but not least, it should be kept in mind that multiple functions of biomaterials are based on animal model studies. We believe that through the interdisciplinary collaboration of experts in the fields of clinical medicine, material science, and nanotechnology, more detailed studies and comprehensive explorations can successfully identify treatments with higher efficiency to aid in the fight against bone tumors.

This review summarizes the very latest developments in the biomaterial-based strategy for bone tumor treatment, with a focus on innovative scaffold design. It also discusses nanomaterials that can help deliver drugs or provide hyperthermia therapy to kill bone tumor cells. In the future, the biomaterial-based strategy may offer unprecedented opportunities for clinical bone tumor therapy and bone regeneration while reducing treatment periods and ultimately improving the prognosis of patients.

Author contributions

YZ reviewed the literature, and wrote the manuscript. YW and XQ wrote and revised the manuscript. TL and YW assisted in drawing. MW designed and revised the manuscript. All authors contributed to the article and approved the submitted version.

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